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PULMONARY COMPLICATIONS OF ACUTE RENAL AND PERIRENAL SUPPURATION*

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THAT acute renal or perirenal infection may occasionally involve the pleura, lung parenchyma and bronchi is generally well known. At times this complication can so obscure the clinical picture that the underlying pathology is discovered with difficulty or is overlooked. More commonly, however, the pulmonary changes are of a relatively minor degree and escape attention unless specifically searched for.

There is little mention in the literature regarding this condition except for the exceedingly few cases of perinephric abscess with bronchial fistula.

The literature devoted to discussion of subphrenic intraperitoneal abscess quite generally recognizes that intrathoracic inflammatory processes constitute the most frequent complications of this lesion. Ochsner and Graves,[1] in reporting an analysis of 3,372 cases of subphrenic abscess collected from the literature, found a 22 per cent incidence of pleural and pneumonic complications. Wellman and Maddock[2] recently reviewed a series of 52 cases of subphrenic abscess, of which one-half showed intrathoracic complications varying from simple pleuritis and pleural effusion to empyema and bronchial fistula. Whereas the literature devoted to subphrenic intraperitoneal abscess invariably emphasizes the importance of transphrenic extension, the literature devoted to extraperitoneal subphrenic suppuration of perirenal origin rarely mentions the complication. In order to determine the incidence and importance of this complication of renal and perirenal suppuration a series of cases was reviewed.

This series is made up of all cases in the University Hospital having a diagnosis of perinephric abscess or pyonephrosis during the thirteen year period of July, 1925–July, 1938. The following cases made up the group:

Pyonephrosis		
Tuberculosis	8	
Non-tuberculous	171	
Total		179
Perinephric abscess		
Tuberculosis	5	
Non-tuberculous	80	
Total		85
Combined total		264

Of the 264 patients, 17 (6.4 per cent) were found to have definite evidence of associated pulmonary or pleuritic pathology. Only 3 (1.7 per cent) of the 173 patients having pyonephrosis showed supraphrenic

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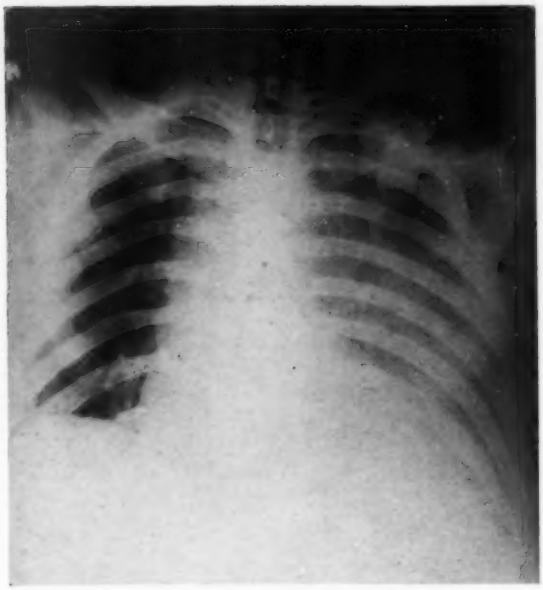

Fig. 1. Case 1. Roentgenogram of chest showing partial obscuration of left lower lung field.

complications, whereas there were 14 such cases (16.5 per cent) in the group of 85 patients with perinephric abscess.

The pathology of the complications varied from a minimal pleuritis to effusion, pneumonitis, and bronchial fistula. Most of the patients showed pleuritic changes only, but 4 probably had pneumonitis of some degree and 6 had perinephro-bronchial fistulae.[3] In all but one patient the changes were evident on roentgen examination of the chest. The one exception (Case VIII) was a patient having perinephro-bronchial fistula in which the positive evidence was established by the clinical symptoms as noted in the case summary. All the patients showed elevation of the diaphragm on the affected side.

REPORT OF CASES

Case 1 (No. 419886). F. N., male, aged twenty-three, was admitted on March 20, 1938, with a history of intermittent attacks of colicky pain in the left costovertebral angle radiating around the flank and down to the penis for fourteen months; severe attack ten days before admittance. He developed fever, nausea, vomiting and mild dyspnea four days previous to admittance. Examination revealed marked tenderness in the left costovertebral region; left diaphragm appeared elevated; râles present at both bases, more pronounced on left; breath sounds not audible at left base. Temperature 103.3° F. Urine grossly infected with bacilli and cocci. White blood cell count 13,800. Blood nonprotein nitrogen 33.8 mg. per 100 cc. Sputum typing negative.

Roentgenogram of the chest on March 21 (Fig. 1) showed obscuration of left lung field, most marked in region of lower lobe. A tentative diagnosis of pneumonia was made and the patient treated on the medical service. On March 28, 200 cc. of sterile fluid was removed from the left chest. Excretory pyelograms of same date (Fig. 2) demonstrated a left calculous pyonephrosis and a right hydronephrosis and hydroureter. After removal of 250 cc. more sterile fluid, a roentgenogram of the chest on March 31 (Fig. 3) showed marked improvement.

On April 2 a left nephrolithotomy and nephrostomy was done. At operation there was definite evidence of a perinephritis but no free pus was encountered. The pulmonary findings cleared up steadily and on April 11 a chest film

Fig. 2. Case 1. Excretory pyelogram showing right hydronephrosis and hydroureter, and left calculus pyonephrosis.

(Fig. 4) revealed only slight residual involvement of the left lower lobe. The nephrostomy tube is still in place. Pyelograms on December 7, 1938, showed definite decrease in the size of the hydronephrosis bilaterally.

Case II (No. 421044). E. J., male, aged forty-one, was admitted on April 7, 1938. He had had a bilateral nephrolithotomy four years previously with good health until two weeks before admittance, when he developed pain in the left flank, fever, nausea and vomiting. On entry he was acutely ill, with fullness and tenderness in

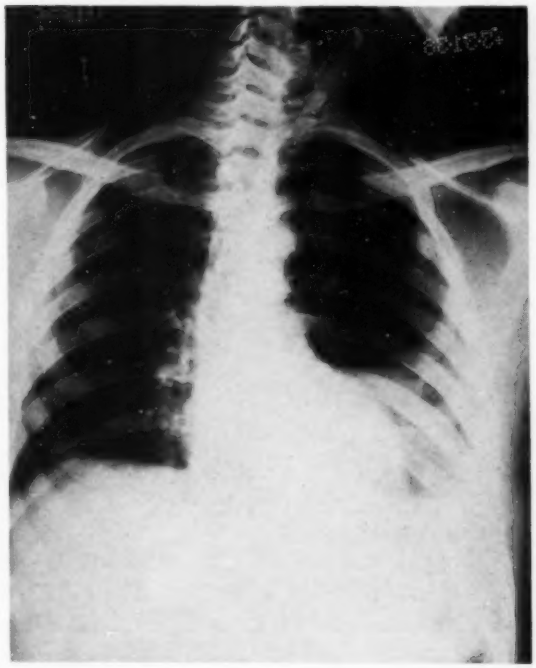

Fig. 3. Case I. Roentgenogram of chest showing improvement following aspiration of fluid from left chest.

left flank. The chest showed dullness to percussion at left base posteriorly, with râles and decreased breath and voice sounds in that region. The temperature was 101.2° F. Urine showed pus but no organisms in the stained sediment. No acid-fast organisms were present. White blood cell count 10,800. Blood nonprotein nitrogen 45.4 mg. per 100 cc.

A bedside chest roentgenogram on April 7 (Fig. 5) showed obscuration of the major portion of the left lung field. There was no displacement of the heart. Retrograde pyelograms on the following day (Fig. 6) revealed a normal right kidney and evidence of cortical destruc-

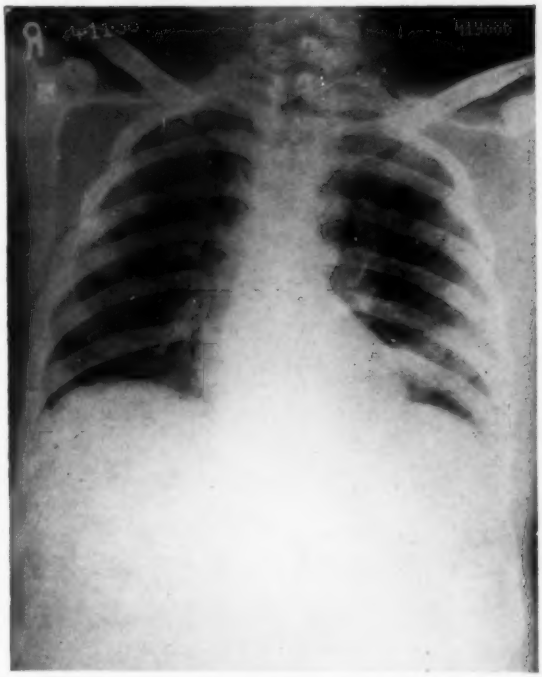

Fig. 4. Case I. Roentgenogram of chest showing marked improvement nine days following drainage of left kidney.

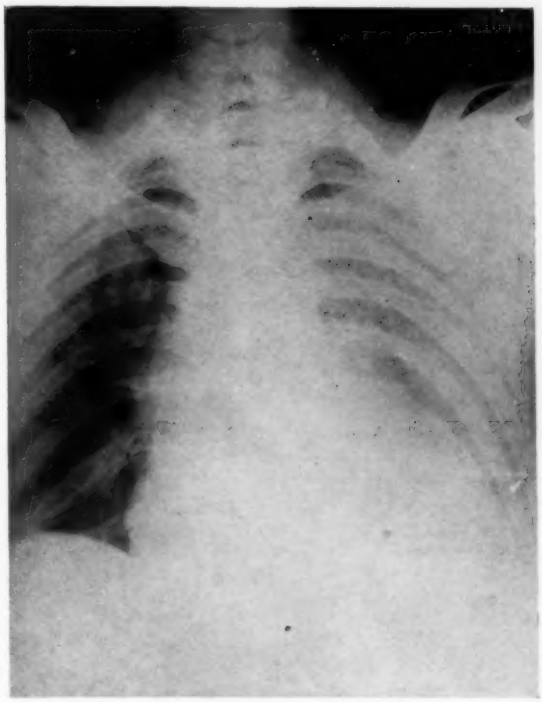

Fig. 5. Case II. Roentgenogram of chest showing obscuration of left lung field on admittance.

Fig. 6. Case II. Retrograde pyelogram showing left nephrocolic fistula.

Fig. 7. Case II. Roentgenogram of chest showing clearing of pneumonitis.

tion in the left kidney and a fistula between kidney and colon. The left ureteral catheter was maintained in position, irrigated frequently and the patient given symptomatic care. On April 9 methylene blue injected through the catheter was recovered in the feces within one hour. Clinically improvement was rapid, and on April 12 a roentgenogram of the chest (Fig. 7) showed some clearing of the inflammatory process in the left lower lung. A left retrograde pyelogram on April 13 (Fig. 8) demonstrated

Fig. 8. Case II. Left retrograde pyelogram showing improvement following prolonged ureteral catheter drainage.

great improvement in the appearance of the kidney and no evidence of nephrocolic fistula. Patient was discharged on May 14 and has not returned, but is reported by his local physician to be well and working daily on his farm.

Case III (No. 422619). H. F., male, aged thirty-four, was admitted on May 5, 1938, with a history of onset of pain in left lower quadrant of abdomen two weeks before admittance with recent development of steady aching pain in the left costovertebral region. Examination on entry showed tenderness in left costovertebral angle. The lung fields were clear except for slight diminution of breath sounds and slight

dullness on percussion at left base. No râles or sputum. Temperature was 102.2° F. Urine was moderately infected with cocci. White blood cell count 24,000. Blood nonprotein nitrogen 36.2 mg. per 100 cc.

A roentgenogram of the chest on May 6 (Fig. 9) showed pleural thickening at the left base and questionable pneumonic involvement and pleural fluid. Retrograde pyelogram on the same day (Fig. 10) showed a left lower ureteral calculus, left hydroureter and hydronephrosis, and evidence of cortical or pelvic rupture.

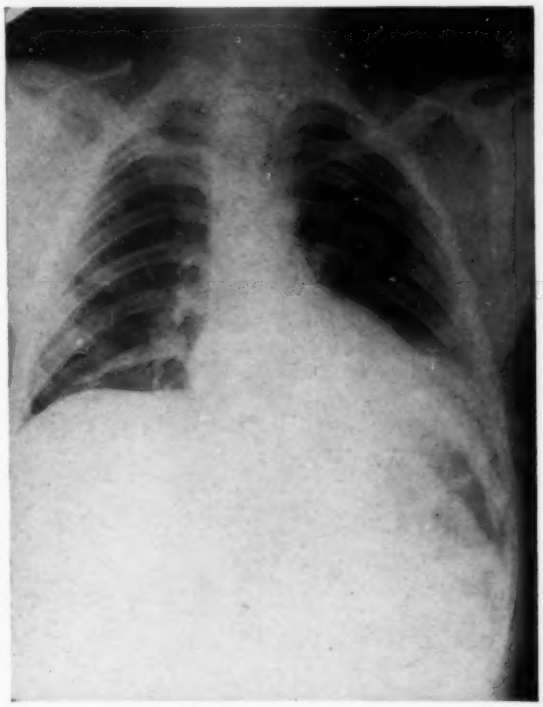

Fig. 9. Case III. Roentgenogram of chest on admittance showing left basilar pleuritis and questionable fluid.

Operation was done on May 6, at which time the perirenal tissues were found to be indurated and edematous; a large amount of extravasated urine was evacuated and the wound drained. The postoperative course was uneventful, the stone passing during the convalescence. A pyelogram on May 25 (Fig. 11) showed a normal left kidney. Unfortunately no postoperative chest films were made but examination of the chest was negative at the time of discharge.

Case IV (No. 270348). G. T., male, aged twenty-six, was admitted on July 25, 1931, complaining of right flank and right abdominal

Fig. 10. Case III. Retrograde pyelograms showing left ureteral calculus, left hydronephrosis and hydroureter, and pelvic or cortical rupture.

Fig. 11. Case III. Normal left pyelogram seventeen days following drainage of left perinephric urinary extravasation.

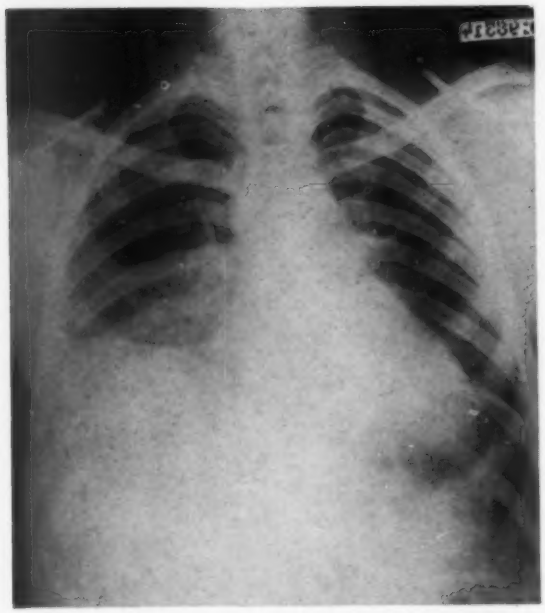

Fig. 12. Case iv. Roentgenogram of chest showing right basilar pleurisy with evidence of fluid and questionable pulmonary infiltration.

pain which had been present for three days. Three weeks before admittance the patient had contracted gonorrhea. Tenderness in the right costovertebral region and right upper quadrant of the abdomen was found on examination; the chest showed dullness beneath the angle of the scapula posteriorly and the fourth rib in front, with increased fremitus and tubular breath sounds; no râles. Temperature was 101.8° F. The urine contained many pus cells and diplococci. White blood count 21,000.

A roentgenogram of the chest on July 27 (Fig. 12) revealed an elevated right diaphragm with definite evidence of fluid in the pleural space and associated obscuration of the lower portion of the middle and lower right lobes. On August 2 a pyonephrotic kidney was drained through an abdominal incision, since under anesthesia there appeared to be a definite mass in the right upper quadrant. Recovery was prompt and on August 26, after the left kidney had been shown to be normal, a right nephrectomy was done through a lumbar incision. Convalescence thereafter was rapid and the patient was discharged on September 20, 1931, at which time the chest was clear on physical examination.

Case v (No. 416173). C. R., male, aged twenty-four, was admitted on January 13, 1938, with a history of having had numerous furuncles during the preceding six months. Since December 24, 1938, he had had pain in the right upper quadrant of the abdomen and in the right flank accompanied by fever, night sweats, and a non-productive cough. Examination showed marked tenderness throughout the right abdomen and in the right costovertebral region. There was a lag in expansion of the right thorax, with dullness on percussion at the right base posteriorly. The right diaphragm appeared fixed, breath sounds over the right base were decreased and râles were heard up to the level of the third rib posteriorly. The temperature was 101.2° F. The urine was normal. White blood cell count 16,150.

Roentgenograms of the chest on January 13 were underexposed but did show an area of increased density at the right base posteriorly which was thought to represent early bronchopneumonic changes. An excretory pyelogram on January 15 (Fig. 13) was diagnostic of right perinephric abscess. The abscess was incised and drained on the same day. The postopera-

Fig. 13. Case v. Excretory pyelogram showing evidence of right perinephric abscess. Fixation of right kidney on inspiration during exposure of this film. The left pyelogram is obscured by respiratory motion; obscuration of right iliopsoas shadow.

tive course was uncomplicated and the patient was discharged on February 4, 1938, feeling well, with chest clear on physical examination.

Case vi (No. 355675). S. Q., female, aged forty-one, entered the University Hospital on October 6, 1935, complaining of pain in the left flank. A tentative diagnosis of left perinephric abscess was made. While the patient was being studied she suddenly had a paroxysm of coughing and raised 95 grams of foul purulent spu-

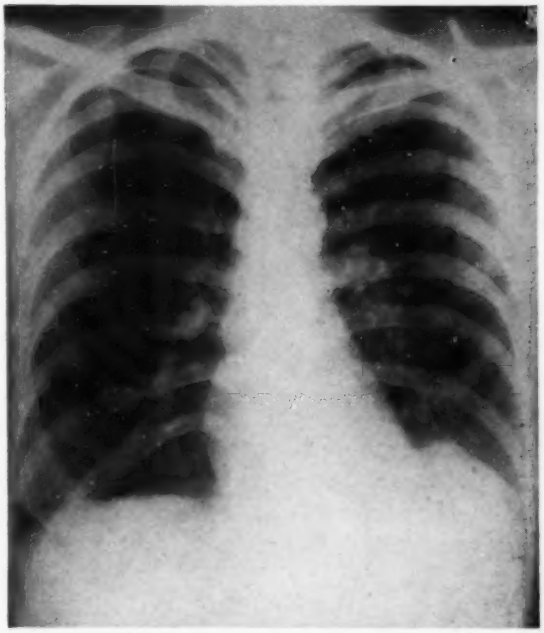

Fig. 14. Case vi. Left perinephro-bronchial fistula; roentgenogram of chest showing tenting of left hemidiaphragm.

tum. A roentgenogram of the chest taken within ten minutes (Fig. 14) showed only tenting of the left diaphragm. Later the patient raised more sputum and a chest film demonstrated a path of pneumonitis from the diaphragm to the hilum, upon which a diagnosis of perinephric abscess with bronchial fistula was made (Fig. 15).

After incision and drainage of the perinephric abscess the patient's convalescence was progressively good and the chest findings gradually returned to normal (Fig. 16).

Case vii (No. 275398). J. B., female, aged thirty-eight, was admitted on September 30, 1931, with a history of constant pain in the right loin accompanied by fever, chills and

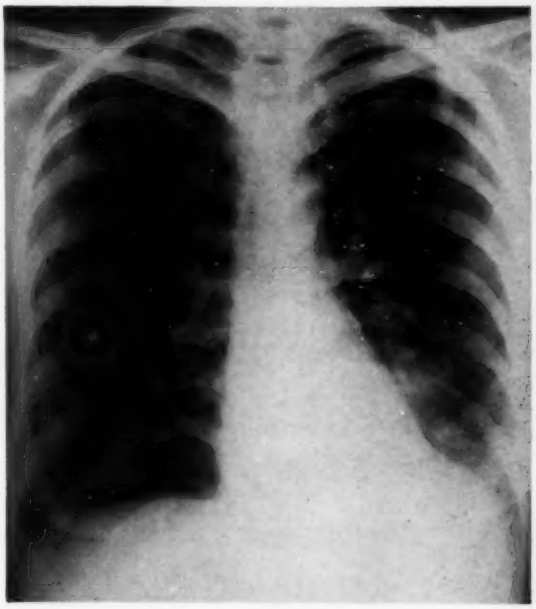

Fig. 15. Case vi. Roentgenogram of chest showing probable fluid in extreme gutter of left base and a path of pneumonitic change from diaphragm to hilum.

weight loss. There was costovertebral tenderness on the right, with elevation of the right diaphragm. Retrograde pyelograms (Fig. 17)

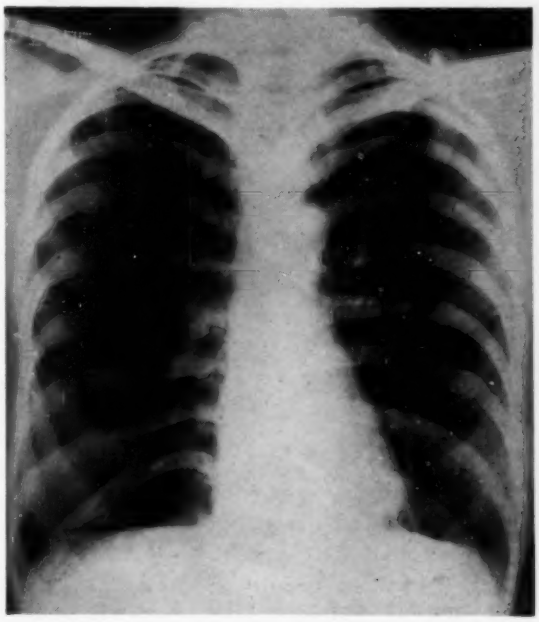

Fig. 16. Case vi. Appearance of chest twenty days following incision and drainage of left perinephric abscess.

Fig. 17. Case vii. Right pyelogram suggestive of neoplasm of renal carbuncle.

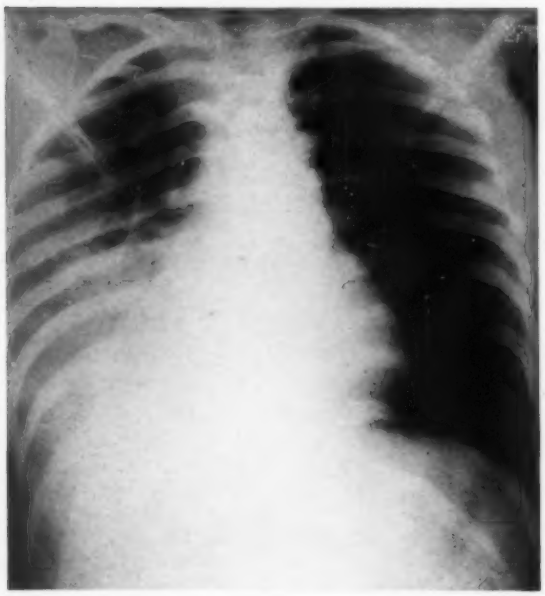

Fig. 18. Case vii. Right diaphragm at fifth costochrondral junction with the lower medial portion obscured by a questionable pneumonic or atelectatic process. Heart shifted to the right. Left lung emphysematous.

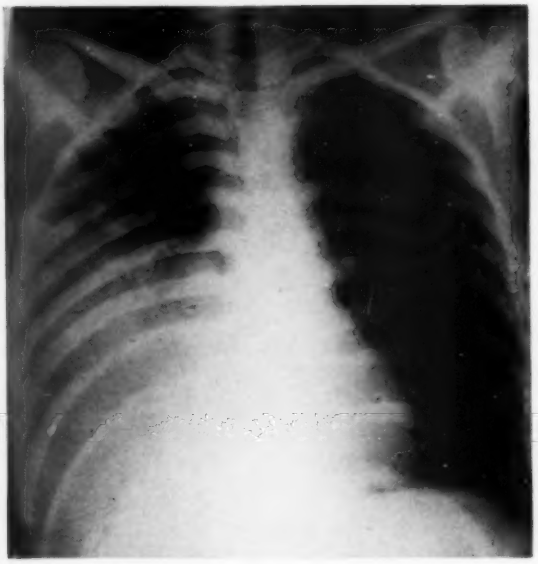

Fig. 19. Case vii. Showing infiltration on the right side up to the second interspace anteriorly.

suggested right renal carbuncle or tumor. Operation was planned but cancelled when the patient suddenly developed a fever of 103° F. with signs of a right basilar pneumonia. A roentgenogram of the chest on the same day showed increased density at the extreme right

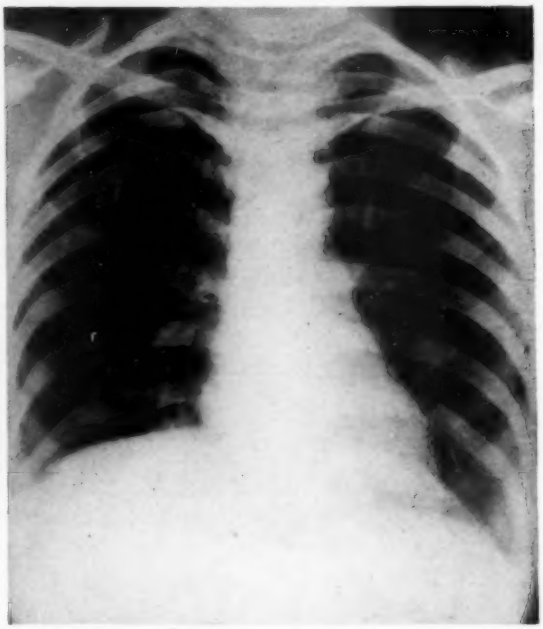

Fig. 20. Case vii. Showing complete regression of pneumonitis and atelectasis.

median base. Two days later roentgenograms of the chest (Fig. 18) showed progression in the obscuration of the right lung. That same day the patient coughed up a large amount of foul sputum and further chest films (Fig. 19) showed infiltration up to the second interspace anteriorly on the right. Incision and drainage of a right perinephric abscess was done immediately, at which time a 2 cm. opening in the diaphragm was found. After a slow but satisfactory convalescence during which the lung cleared up completely (Fig. 20) the patient was discharged on January 12, 1932.

Case VIII (No. 149676). F. B., male, aged twenty-eight, was admitted on July 27, 1926. He had previously had a large right perinephric abscess drained in January, 1925, and redrained in January, 1926. A draining sinus persisted. Examination showed a tender mass in the right upper quadrant of the abdomen and high fixed right diaphragm. A diagnosis of recurrent perinephric abscess was made and drainage established. Postoperatively the wound was irrigated daily with acriflavine. On two occasions, August 15 and 19, 1926, large amounts of acriflavine were coughed up while the wound was being irrigated, thus proving the existence of a perinephro-bronchial fistula. Roentgen studies failed to visualize the course of the fistula.

Later pyelograms showed characteristics of right renal tuberculosis but the patient refused nephrectomy and was discharged on August 21, 1926.

CONCLUSIONS

1. It appears from this series that perirenal suppuration is not uncommonly complicated by extension above the diaphragm —an incidence of 16.5 per cent occurring in this group.

2. Delay in diagnosis of perirenal suppuration seems to influence importantly the occurrence of these complications.

3. Pleural or pneumonitic complications of renal or perirenal suppuration may overshadow the symptoms and signs of the latter and cause unwarranted delay in their surgical treatment.

4. Except in the presence of a frank empyema or pulmonary abscess the treatment of the pulmonary complications of renal or perirenal suppuration consists of an adequate drainage of the primary lesion.

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ROENTGEN RECOGNITION OF SYNOVIOMA

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IN a small series of 4 cases, an unusual and striking roentgen appearance has been found in each instance to indicate a synovioma, or synovial sarcoma, either malignant or with potential malignancy. The whole subject of synovioma is being studied at this time by the pathologist of this hospital, Dr. Dominic A. DeSanto, who will shortly write more comprehensively of this subject. In the meantime, it seems advisable to call to the attention of the medical profession this striking roentgen manifestation and its dangerous implication.

In Dr. DeSanto's series, this unique, and apparently pathognomonic roentgenographic appearance was found in about 25 per cent of the cases. Near a joint, and sometimes involving the joint, is seen a rounded, sometimes rather lobulated, sharply defined soft tissue tumor mass. No differential diagnosis can be made on such a mass in itself; but when in the mass is found a scattered and irregular deposit of amorphous lime, we have learned that a provisional diagnosis of synovioma is justified.

In our limited experience with this manifestation, we have thus far found no other condition simulating it. The calcifications in angiomas are very orderly and in the characteristic form of phleboliths. Exostoses and osteochondromas are more extensively calcified, and with the pattern of orderly bone throughout, except in their cartilaginous caps where the lime deposit may be quite irregular.

CASE REPORTS

Case 1. L. A. M., male, aged twenty-four. Patient was seen at the Hospital for Ruptured and Crippled on October 16, 1935. Six years ago he fell down a flight of stairs and had some swelling in the left knee following this. A short time later he was kicked in the left knee, and since that time he has had some pain and discomfort on the lateral aspect of this joint. For the past three or four years he has had considerable pain and stiffness in this leg.

Examination showed a tender swelling over the lateral aspect of the left knee. There was no instability. No fluid was found in the joint. The range of motion was from 90–160 degrees.

Stereoscopic roentgen examination of the left knee (Fig. 1) showed a large, sharply defined, irregularly calcified body lying posterior to the lateral femoral condyle, reaching as high as the level of the popliteal space, and as low as the lowermost point of the lateral femoral articular surface. This calcified body dipped into the intercondyloid notch mesially, and extended at least one-third of the distance toward the front of the joint. The joint was believed to be involved.

Operation November 4, 1935. A tumor about 2½ inches in diameter was excised. It was irregularly lobulated, did not seem to be adherent, and was quite easily dissected out.

Pathological examination at that time did not arouse serious suspicion of malignancy, and the mass was regarded as a chronic productive bursitis showing calcification, chondrification, and ossification.

October, 1936. There was a recurrence of symptoms, and examination showed a recurrence of the tumor. A review of the previous slides by Dr. DeSanto and other pathologists, in view of the recurrence, brought the diagnosis of an unusual form of synovial sarcoma.

Deep roentgen therapy was given at Memorial Hospital. Amputation was then advised, but refused. Shortly thereafter, the patient consulted a Boston physician. The recurrence was excised, and was found to be frankly malignant. Amputation was advised and accepted, and performed at Massachusetts General Hospital on February 13, 1937. Pathological report at that hospital: sarcoma, type undetermined, ? synovioma.

Subsequent comparison by Dr. DeSanto of

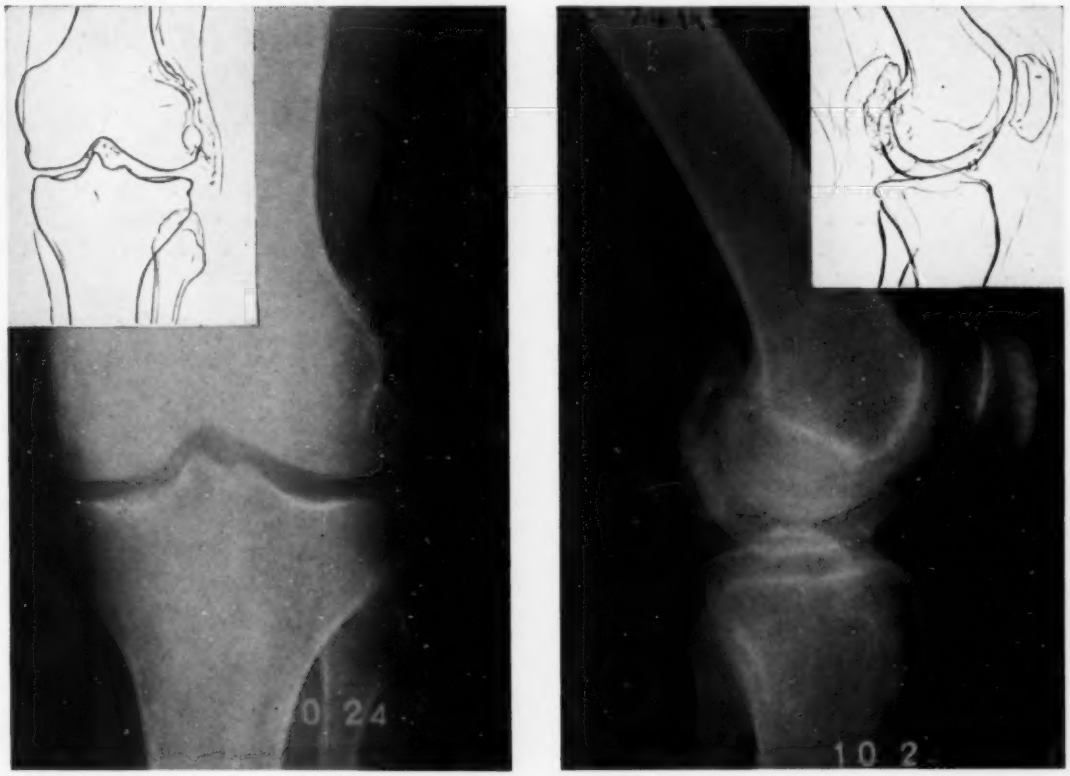

Fig. 1. Case 1.

the tissue from this case with the later cases of synovioma, taking into consideration the many clinical similarities, brought the conclusion that this was a true example of synovial sarcoma. In February, 1939, roentgenograms showed pulmonary metastasis. Death from metastasis September 4, 1939. Autopsy not permitted.

Case II. G. B., male, aged twenty-two. Admitted to the Hospital for Ruptured and Crippled September 14, 1938, with complaint of painful mass on the lateral aspect of the left lower thigh.

Three years ago patient was spiked on the lateral aspect of the left lower thigh while playing football. There was immediate swelling and pain which subsided under rest and hot compresses. About three months later pain and swelling reappeared, and increased gradually during eight months. A physician was consulted, roentgenograms were taken, and he was admitted to a Brooklyn hospital, where the mass was excised September 11, 1936. The mass was of the consistency of soft bone, measured 5×2.5 ×2.5 cm., and was found involving the musculature and extending back to the popliteal space. The pathologist of this hospital suspected osteogenic sarcoma, but other pathologists considered it benign. There was a recurrence of the pain and mass three months after operation, and the mass has grown slowly during the past year.

Examination on admission to the Hospital for Ruptured and Crippled showed a limp on the left. There was a fairly well circumscribed tumor on the lateral aspect of the thigh just above the knee, with a linear scar over it. The mass measured about 7 cm. in diameter, was firmly attached to the deeper structures, but not to the skin, it was of varying consistency, and very tender posteriorly.

Roentgen examination (Fig. 2) showed a lobulated soft tissue mass on the lateral aspect of the lower thigh, extending from the level of the femoral epiphyseal line upward a distance of approximately 13 cm. There was an irregular distribution of lime in it in a faintly lobulated pattern. There was no evidence of bone involve-

ment, with the possible exception of a little pressure atrophy.

Operation, September 16, 1938, excision of tumor. Tumor mass was in the substance of the vastus lateralis. Wide excision with the surrounding soft tissues was performed.

After prolonged study of the excised tissue, a pathological diagnosis of synovial sarcoma was made. Dr. DeSanto believes the tumor is aggressive, and that dissemination of the disease is inevitable without further treatment.

Follow-up: A report from the Social Service Department in October, 1939, indicated that the patient was working and was apparently in good health.

Fig. 2. Case II.

Case III. A. S., female, aged thirty-four, came to the clinic at the Hospital for Ruptured and Crippled March 28, 1939, with a complaint of swelling just above the left wrist. Five or six years ago she noticed the swelling, which had increased in size slowly. No history of trauma. No pain.

Examination showed a nodular, not very firm swelling anteriorly and posteriorly, just above the wrist. Left forearm 1 inch proximal to wrist measured 8 inches, right $7\frac{1}{4}$ inches. Wrist motion normal. Atrophy of hand muscles, with weak grip.

Roentgen examination (Fig. 3) showed a sharply defined, rounded soft tissue tumor mass, situated between the radius and ulna. It started just above the lower radio-ulnar articulation and extended up the forearm a distance of about 4 cm. It bulged both anteriorly and posteriorly, and contained a rather irregular deposition of lime. There appeared to be a certain amount of pressure atrophy from this mass on the lower ulnar shaft. Roentgen diagnosis: probably synovioma.

Patient went to a hospital in Brooklyn, where the mass was excised on April 6, 1939. The mass was circumscribed, about 4 cm. in diameter. The tissue was examined by Dr. DeSanto, who made a diagnosis of synovioma.

November 20, 1939, the patient was well without evidence of recurrence.

Case IV. E. P., male, aged thirty. This case is included through the courtesy of Dr. Francis

Fig. 3. Case III.

J. Fadden, Jr., and Dr. DeSanto. The patient was admitted to the Englewood Hospital, Englewood, N. J., on May 2, 1939, and operated upon for acute appendicitis. He also gave a history of gradually increasing difficulty in flexing and extending the right elbow, and of a sense of fullness in the antecubital region.

Examination showed a marked prominence of the anterior surface of the flexor group of muscles overlying the anterior surface of the elbow joint. Elbow motion was from 90–135 degrees.

Roentgen examination (Fig. 4) showed a circumscribed soft tissue shadow extending to the humeroulnar articulation, containing small foci of calcification.

Operation at the Englewood Hospital May 9, 1939. Tumor mass was shelled out, leaving a perfectly clean base.

Pathological report: synovial sarcoma.

The patient refused to consider amputation, and was difficult to follow-up. He was seen November, 1939, at which time discrete nodular masses were present in both axillae. Roentgenograms of the chest were negative. He refused further treatment.

Fig. 4. Case IV.

COMMENT

Four cases with unusual and similar roentgenographic findings were found to be synoviomas, or synovial sarcomas. Two of these developed clinical evidence of malignancy. The other two, although regarded as malignant or potentially malignant from the pathological viewpoint, had not shown recurrence or metastasis thirteen and seven months after operation, respectively.

CONCLUSIONS

1. Four cases are described and illustrated in which distinctive and essentially identical roentgenograms were found to indicate malignant, or potentially malignant, synoviomas or synovial sarcomas.

2. This distinctive roentgen finding seems to occur in about 25 per cent of synoviomas.

3. Thus far, no other pathological condition giving similar roentgen findings has been encountered.

4. Whenever roentgenograms similar to those described are encountered, a provisional diagnosis of synovial sarcoma is justified, and the probability of malignancy should be borne in mind.

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CALCIFICATION IN ABDOMINAL NEUROBLASTOMA

REPORT OF TWO CASES*

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CALCIFICATION, and its roentgenological recognition, which has occurred in 2 of our 6 cases of abdominal neuroblastoma, should be emphasized as an aid to diagnosis, especially in children. In the literature on neuroblastoma of the abdomen, although calcification often has been reported by pathologists,[1,5,10,11] it apparently has been demonstrated roentgenologically in only one previous case.[7]

CASE 1 (No. 85031). G. D., white male, aged two, was admitted to Duke Hospital on May

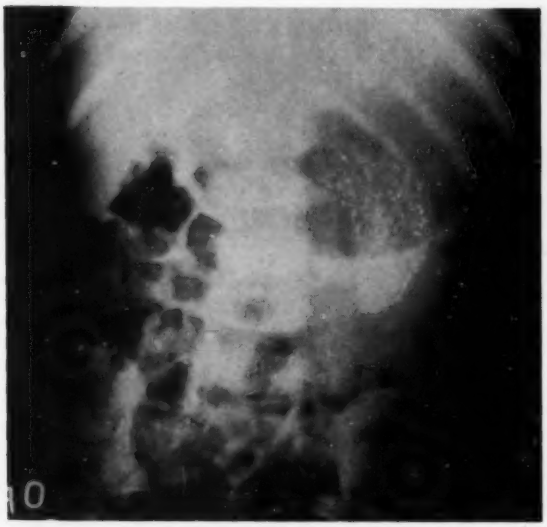

FIG. 1. Case 1. Appearance of the abdominal tumor before operation. (Slightly retouched.)

24, 1937, with a history of pain in the lower spine associated with tenderness over the left hip, which had developed suddenly twenty-four days previously. Roentgen studies of the spine and hips before admission were said to have been negative. Except for a firm, rounded, non-tender mass, the size of an orange in the left flank, and pain on passive motion of the left thigh and pain on pressure over it and the lumbar spine, the results of the physical examination were negative. The blood pressure was 90/45 mm. of mercury; red blood cell count 3,600,000; white blood cell count 9,800, with a normal differential count; hemoglobin 62 per cent (Sahli); urine and stool examinations, and

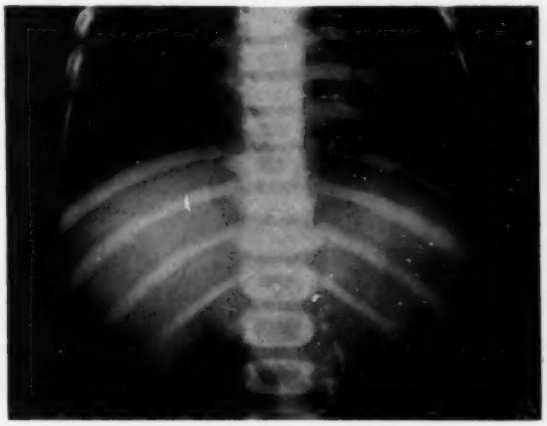

FIG. 2. Case 1. Small amounts of calcium remaining after removal of the main body of the tumor. (Retouched.)

intradermal tuberculin (0.1 mg.) and Wassermann reactions negative, non-protein nitrogen 37 mg. per 100 cc.; calcium (serum) 9.7 mg. per 100 cc.; and (phosphorus plasma) 5.1 mg. per 100 cc. Roentgenograms of the abdomen showed a large soft tissue mass in the left upper quadrant which contained many irregular opaque flecks (Fig. 1). These were interpreted as areas of calcification in a tumor of the left kidney or adrenal. Roentgenograms of the bones and chest showed no metastases. An intravenous pyelogram showed the kidney pelvis to be distorted, apparently by pressure from the tumor mass. The clinical impression was malignant tumor of the left kidney or adrenal. On June 2, 1937, ten days after admission, Dr. Paul W. Sanger, to whom we are indebted for permission to report this case, removed a large retroperitoneal tumor from the left upper quadrant.

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Fig. 3. Case II. The large mass in the left upper quadrant showing extensive calcification. (Retouched.)

It had no apparent connection with the kidney or adrenal, was purplish-red, soft and friable, and had small grayish-yellow nodules throughout the mass. These proved to be the calcified areas seen in the roentgenogram. Microscopically, the tumor was composed of masses of round cells with large nuclei, many typical rosettes, numerous areas of necrosis, hemorrhage, and calcification. The pathological diagnosis was neuroblastoma.† Postoperatively the patient received roentgen therapy. Two weeks later a slight left exophthalmos developed. Repeated roentgenograms of the skull, lungs and spine were negative, but a few small flecks of calcium could still be seen in the region of the left kidney, indicating that the entire tumor had not been removed (Fig. 2). The main body of calcium, however, had disappeared. The patient was discharged in fair condition on June 25, 1937, twenty-three days after the operation. He subsequently died, but no details are known.

Case II (No. 50030). P. P., white female, aged six, was admitted to Duke Hospital on March 15, 1935, with a history of pain in the left abdomen, anorexia and frequent vomiting for the preceding year. Five months after onset, her cervical lymph nodes became enlarged. Nine months after onset, she had influenza, and she remained in bed until admission, three months later. Weakness and weight loss became pronounced, and the abdominal swelling and pain had increased. Ten months after onset, she had a generalized convulsion and became blind for two days. Eleven months after onset the parents noticed an abdominal tumor. Three roentgen treatments over it did not cause any regression.

Physical Examination. On admission, the patient was a well developed, but emaciated and pale girl, who appeared chronically ill. The blood pressure was 125/80 mm. of mercury. The temperature was 38° C. The pulse and respirations were slightly elevated. There was a mass in the left posterior triangle of the neck composed of chains of moderately enlarged lymph nodes. The other cervical lymph nodes also were enlarged, but they were not matted nor tender. Both leaves of the diaphragm were markedly elevated. The abdomen was distended and the superficial veins were very prominent. The liver was enlarged and extended to the level of the umbilicus. A hard mass extending from the costal border to the left iliac crest, filled the entire left side of the abdomen; several small firm nodules could be felt in the epigastrium superficial to the main mass. There was no ascites. The red blood cell count was 2,550,000; white blood cell count 9,200, with a normal differential count; hemoglobin 40 per cent (Sahli); urine and stool examinations and intradermal tuberculin (0.1 mg.), Wassermann and van den Bergh reactions negative; and nonprotein nitrogen 27 mg. per 100 cc. Roentgenograms of the chest demonstrated markedly ele-

Fig. 4. Case II. The metastatic lesions in the pelvis and femoral heads.

† We are indebted to Dr. Sydney Feyder, Dr. H. M. Schiebel, and Dr. A. J. Gill of the Department of Pathology for the pathological data in both cases.

vated diaphragms, a large amount of fluid at both bases, and enlarged left tracheobronchial lymph nodes. Roentgenograms of the abdomen showed a tremendous mass with numerous areas of calcification filling the entire left half of the upper abdomen (Fig. 3). Roentgenograms of the bones revealed irregular areas of decreased density in the pelvis and heads of the femurs (Fig. 4). One of the cervical lymph nodes, which was removed for microscopic study, had extensive necrosis, dark staining tumor cells with large nuclei, and many typical rosettes. The pathological diagnosis was neuroblastoma. Because of the widespread metastases, the abdominal tumor was not removed. The patient was discharged five days after admission, and died one month later.

SUMMARY

1. Two cases of neuroblastoma of the abdomen, in which calcification occurred, are reported.

2. Roentgenologic evidence of calcification, when combined with other clinical data, is useful in the differential diagnosis of intra-abdominal neoplasms, and should help make a diagnosis of neuroblastoma possible before metastatic lesions have occurred.

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CAUSES OF FAILURE OF LUNG EXPANSION FOLLOWING THORACOTOMY FOR ACUTE POST-PNEUMONIC EMPYEMA

WITH SPECIAL REFERENCE TO BRONCHIAL OBSTRUCTION*

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THE roentgenologist is frequently called upon to render an opinion as to the cause of failure of the lung to expand following surgical intervention for empyema. His ingenuity is often taxed to the utmost in attempting to interpret the pathologic processes taking place in the collapsed lung—and even more when the lung is partly obscured by pleural effusion. However, by a knowledge of the underlying possibilities and the modus operandi of each, the interpretation of such roentgenograms becomes simpler.

Pleurotomy as a therapeutic measure in the treatment of empyema thoracis has come to be regarded as one of the milestones in surgery. There still remains, however, a difference of opinion as to the relative merits of any one mode of this procedure over those of the others; but regardless of the method employed, strict adherence to the basic principles enunciated by Graham and his coworkers is essential. It is universally agreed that the cure of an empyema cannot be effected unless the pus is evacuated at the optimum time, the pleural cavity is sterile, the lung is completely expanded and the pleural space is obliterated. Assuming then that drainage was instituted at the proper time and that it is adequate, the failure of the lung to expand following thoracotomy for empyema may be due to one or more of several causes. The source of these causes may be inherent (*a*) in the chest wall, (*b*) in the pleura or pleural cavity, (*c*) in the lung, or (*d*) in the bronchi. In this article 2 cases will be considered in which bronchial obstruction was the cause of delay in the cure of empyema.

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Bronchial obstruction as the cause of the failure of the lung to expand following thoracotomy for empyema has been referred to by many writers. However, no cases have been noted in the literature prior to 1928, when Butler presented his first case. Since that time he has reported 5 cases. It is interesting to note that, except for these cases, none could be found in the literature.

CASE 1. The patient was a white female, aged fifteen, who entered the hospital on the fourteenth day after the onset of a left lower lobe pneumonia. A roentgenographic study of the chest shortly after admission revealed a massive pleural effusion occupying the left hemithorax (Fig. 1). A thoracentesis was performed the day after admission. Bacteriologic examination of the fluid thus obtained showed *Streptococcus viridans*. On the twenty-first day of the patient's illness (Chart 1, A) a thoracotomy (rib resection drainage) was performed. The preoperative temperature which was around 102.6°F. fell steadily to the third postoperative day, when it reached 99.6° F. The patient's general condition appeared improved, the drainage by the tube was satisfactory and copious, but in spite of this on the fourth postoperative day the temperature began to rise. A roentgenogram of the chest taken on the sixth postoperative day showed a residual collection of fluid at the left base, partial expansion of the lung, and some infiltration of the left lower lobe (Fig. 2). From the fourth to the thirty-ninth postoperative day the temperature remained irregularly elevated, fluctuating between 98.6 and 103° F. There was apparently adequate drainage through the thoracotomy, but the patient did not appear to derive as much benefit from this procedure as usual. The convalescence was slow and poor. Roentgenographic studies on the thirteenth and twenty-second postoperative days (Figs. 3 and 4)

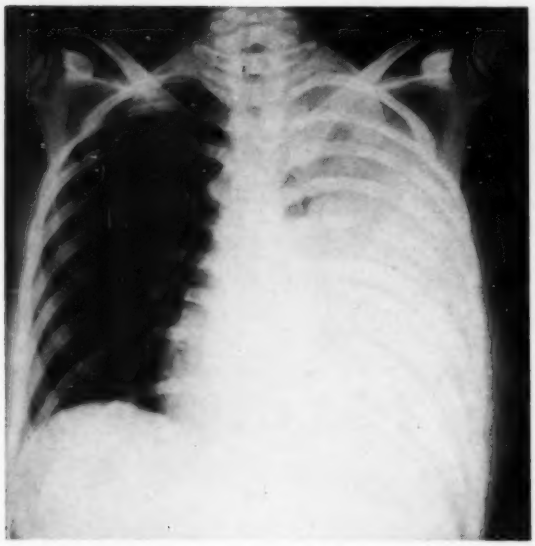

Fig. 1. Case 1. Roentgenogram taken on July 25, 1935 (day after admission to hospital). There is a massive pleural effusion occupying the left hemithorax. The heart is somewhat displaced to the right.

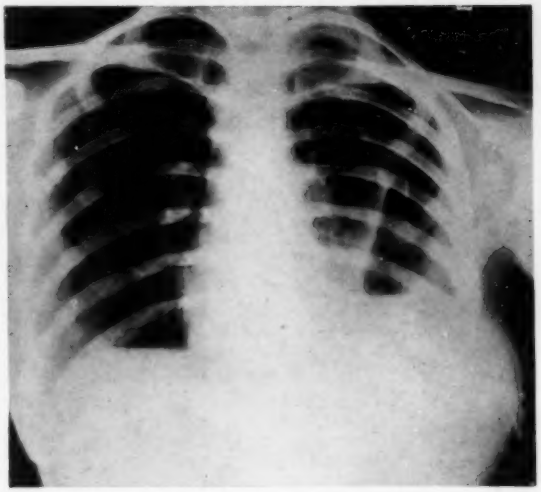

Fig. 2. Case 1 Roentgenogram taken on August 5, 1935 (sixth postoperative day). There is a hydropneumothorax on the left. The fluid extends up to the level of the ninth rib in the paravertebral region. Both lobes are readily visible. There is some infiltration of the left lower lobe. The heart is still somewhat displaced toward the right.

failed to show any appreciable change from those noted on the sixth postoperative day. The fluid in the pleural cavity was slightly diminished, but the expansion of the lung had not increased, nor had there been any change in the infiltration of the left lower lobe.

It was thought that there might be an encapsulated empyema hidden behind the heart,

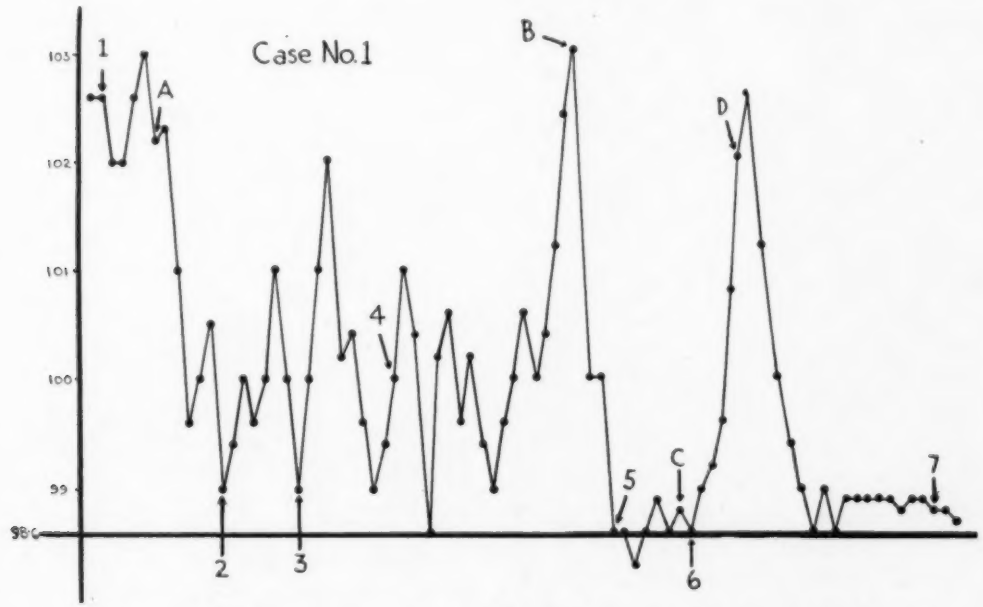

Chart 1. Case 1. Average daily temperature during patient's hospital stay. The numbers on the graph refer to the day on which the corresponding numerical roentgenogram was taken. A, rib resection thoracotomy drainage instituted. B, patient expectorated mucus plug. C, wound stopped draining and closed spontaneously. D, reinsertion of drainage tube.

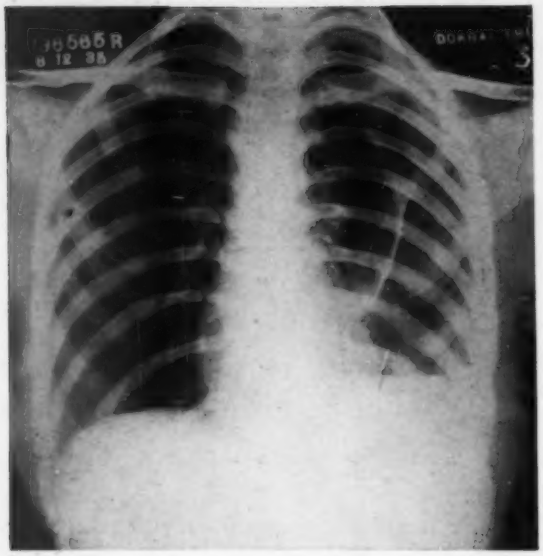

Fig. 3. Case 1. Roentgenogram taken on August 12, 1935 (thirteenth postoperative day). Condition is essentially the same as noted on the previous roentgenogram except that the fluid is at a lower level.

which was responsible for this atypical course. Roentgenographic studies in the oblique, erect and prone positions presented no evidence of any such condition. Up to this time there was apparently adequate drainage of the empyema. On the thirty-fifth postoperative day, because of the patient's poor convalescence, persistent temperature, and incomplete expansion of the lung, a diagnosis of bronchial obstruction was made. It was suggested that the cause was an atelectasis due to retained secretions, and that the temperature was due to a pneumonitis distal to the point of obstruction. Bronchoscopy was advised but was not performed. Four days later (Chart 1, B) the patient was suddenly seized with a cough and expectorated a blood-stained mucoid plug. This was followed by bronchorrhea for several days. The day after the patient had expectorated the mucus the temperature fell from 103 to 100° F., and three days later it dropped to normal. The general clinical improvement in the patient during these three days was remarkable. A roentgenogram at this time showed some opacity along the axillary region of the left hemithorax, but no further expansion of the lung (Fig. 5). Five days later (on the forty-eighth postoperative day), because of the maintained

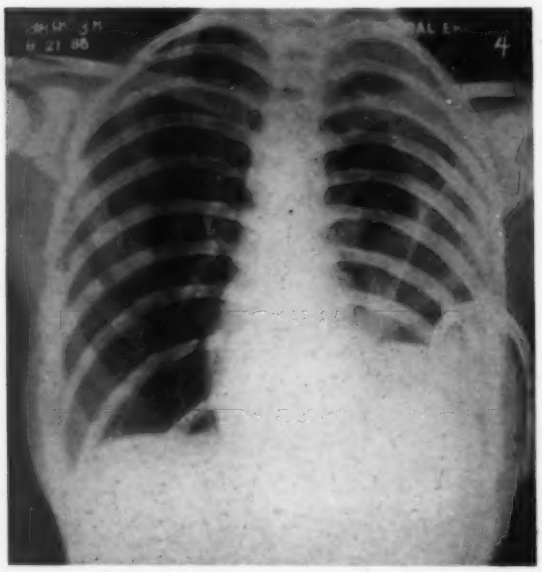

Fig. 4. Case 1. Roentgenogram taken on August 21, 1935 (twenty-second postoperative day). Condition is essentially the same as noted on the previous roentgenogram. The left lower lobe does not appear any further expanded than in the previous two roentgenographic studies.

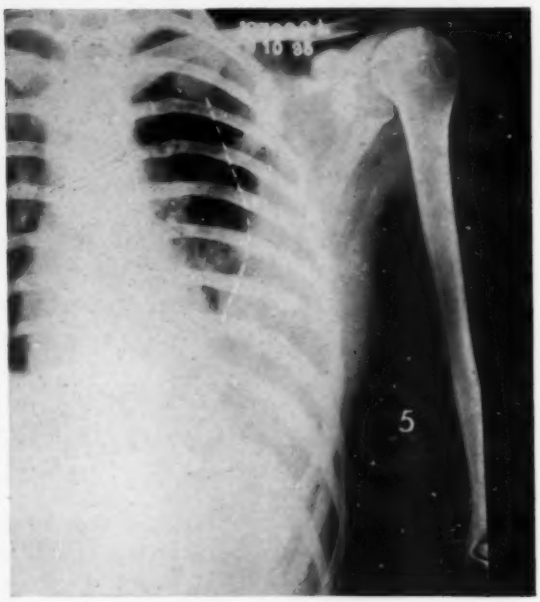

Fig. 5. Case 1. Roentgenogram taken on September 10, 1935 (forty-second postoperative day and three days after expectorating a mucous plug). There is an opacity along the lateral border of the left thoracic cage. There is no further expansion of the lung as compared with that of the previous roentgenogram.

afebrile course, general well-being of the patient, and relatively small amount of fluid in the pleural cavity, the drainage tube was removed. The patient continued to improve steadily, and the wound closed spontaneously (Chart 1, c). A roentgenogram made on the eighth day of normal temperature showed a peripheral collection of fluid with some degree of pulmonary expansion (Fig. 6). The following day the temperature began to rise again, and within a few days it rose to 102° F. A drainage

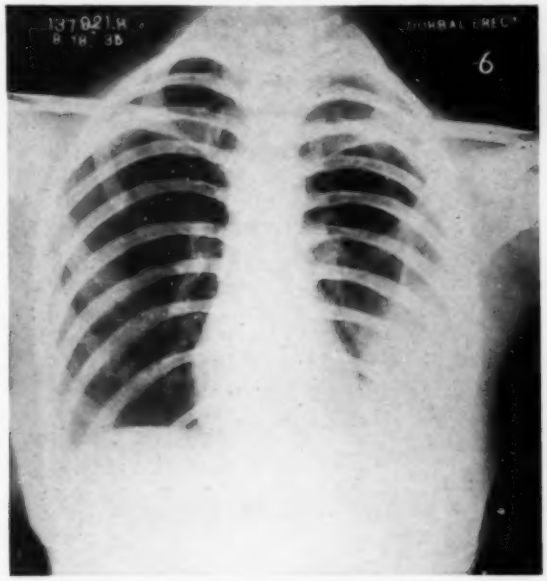

Fig. 6. Case 1. Roentgenogram taken on September 18, 1935 (forty-ninth postoperative day and ten days after expectorating the mucous plug). There is an increase in the expansion of the left lung. There is also present a peripheral accumulation of pleural fluid.

tube was re-inserted through the old thoracotomy site (Chart 1, d) and the pus evacuated, following which the temperature dropped to normal as though by crisis. A roentgenogram made about two weeks after the temperature dropped to normal showed further expansion of the lung (Fig. 7). Another roentgenogram made three weeks after the patient's discharge from the hospital showed complete expansion of the lung, and no reaccumulation of the pleural fluid (Fig. 8).

Case II. The second case is that of a boy, aged three, who entered the hospital with a seven-day history of a left lower lobe pneumonia. A thoracentesis performed on the day

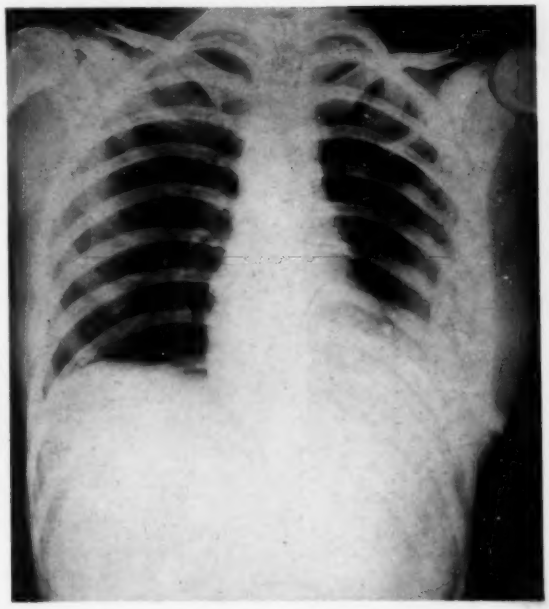

Fig. 7. Case 1. Roentgenogram taken on October 8, 1935 (seventy-first postoperative day). The lung is further expanded. There is some opacity along the axillary region of the left hemithorax which is due to thickening of the parietal pleura and possibly a small amount of retained fluid.

of admission revealed a thick, grayish, purulent exudate which on bacteriologic examination showed *Streptococcus haemolyticus* and pneu-

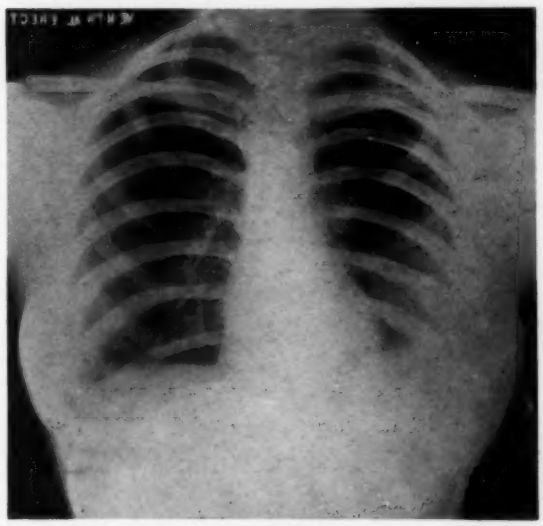

Fig. 8. Case 1. Roentgenogram taken on November 1, 1935 (three weeks after discharge). There is complete expansion of the lung. Some thickening of the pleura on the left side still obtains.

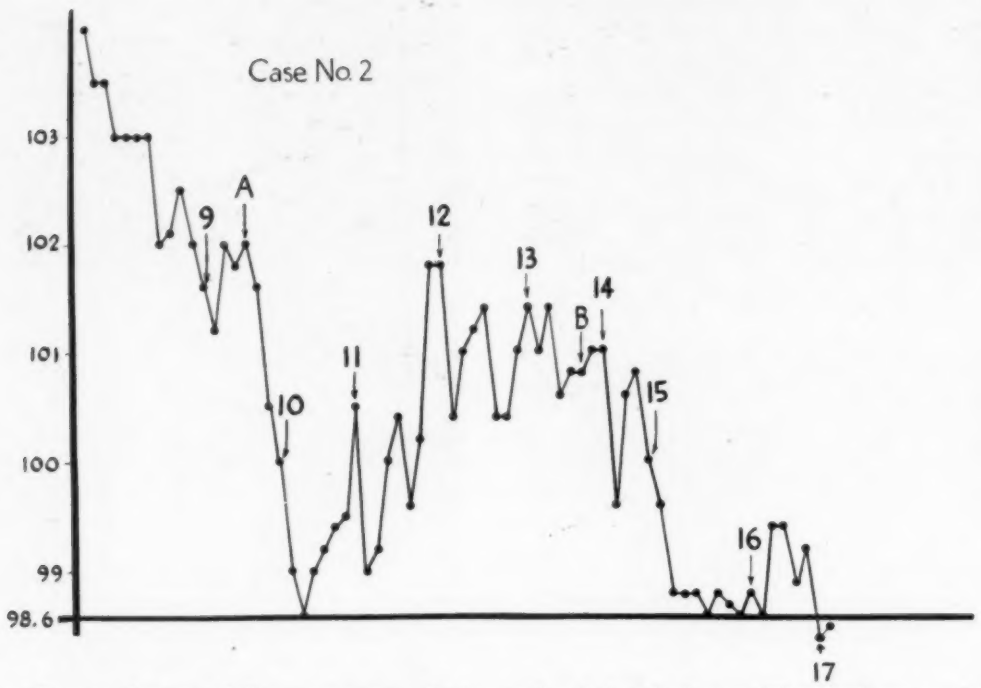

Chart II. Case II. Average daily temperature during patient's hospital stay. The numbers on the graph refer to the day on which the corresponding numerical roentgenogram was taken. A, rib resection thoracotomy drainage instituted. B, patient expectorated mucous plug.

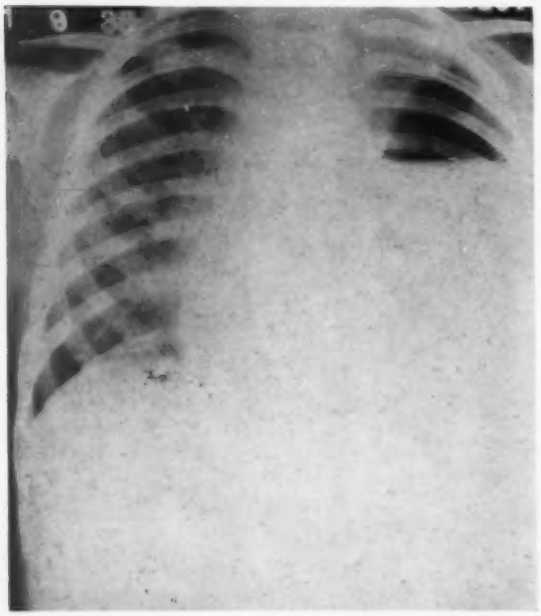

Fig. 9. Case II Roentgenogram taken on November 9, 1938 (four days before thoracotomy was performed). There is a hydropneumothorax of the left side with incomplete collapse of the lung. The mediastinal structures are displaced toward the right.

mococcus. A roentgenogram made on the nineteenth day of illness showed a hydropneumothorax on the left with displacement of the mediastinal structures toward the right (Fig. 9) On the twenty-third day of illness (Chart II, A) a rib resection thoracotomy, for the drainage of the empyema, was performed. The immediate postoperative course was satisfactory. The preoperative temperature, which was 102.2° F., fell so that on the fifth postoperative day it was normal. A roentgenographic examination of the thorax on the third postoperative day showed a diffuse opacity of the left hemithorax; the mediastinum was reposited in its normal position, and about two-thirds of the lung was expanded (Fig. 10). On the sixth postoperative day the temperature began to rise, and on the tenth day it was 100.5° F. The patient's condition appeared poor; he was listless and refused food. The drainage tube was apparently functioning satisfactorily, and no explanation could be offered for the patient's status. A roentgenogram of the chest made this day showed some clearing of the left apical region (Fig. 11). The lower half of the left chest was still radiopaque. Comparison of this roentgenogram with the previous one showed the

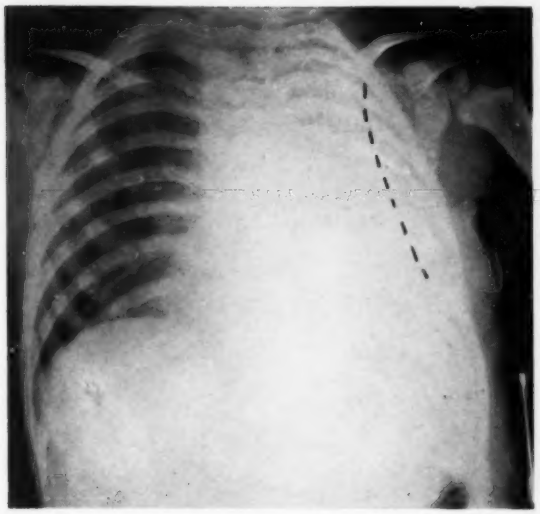

Fig. 10. Case 11. Roentgenogram taken on November 16, 1938 (third postoperative day). There is a diffuse opacity of the left hemithorax, part of which is due to the overlying dressing. The mediastinal structures appear replaced in their apparently normal position. About two thirds of the left lung is re-expanded.

lung to be somewhat more infiltrated but not any more expanded.

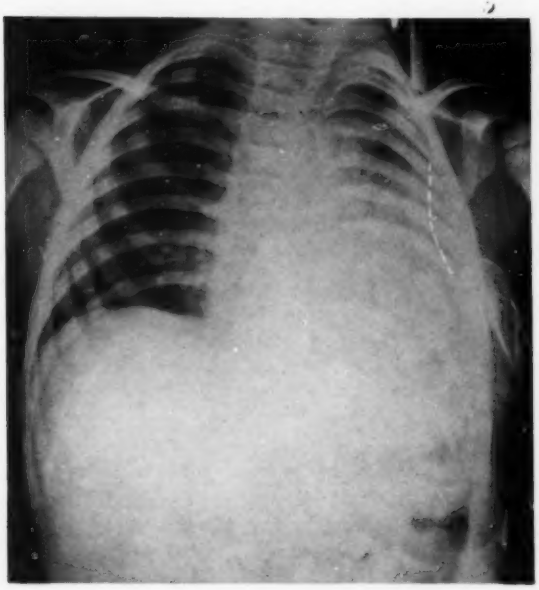

Fig. 11. Case 11. Roentgenogram taken on November 23, 1938 (tenth postoperative day). There is some clearing of the left apical lung field. The lower part appears opaque and infiltrated. There is present a partial pneumothorax which extends along the lateral third of the hemithorax.

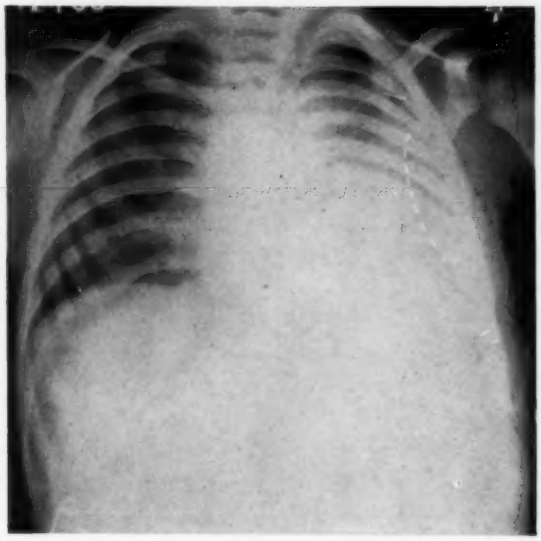

Fig. 12. Case 11. Roentgenogram taken on December 1, 1938 (eighteenth postoperative day). Except for some further clearing of the apex, the condition is essentially the same as noted on the previous roentgenogram.

For the following eight days the temperature continued intermittently elevated, and on the seventeenth and eighteenth postoperative days it reached 101.8° F. Drainage by the thoracotomy tube was profuse. The patient was listless and non-cooperative. A roentgenogram made on the eighteenth postoperative day

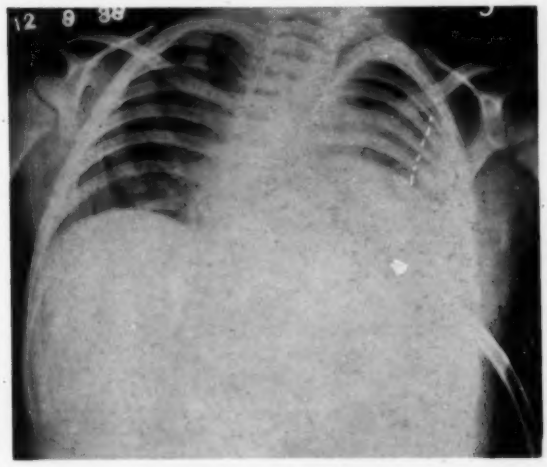

Fig. 13. Case 11. Roentgenogram taken on December 9, 1938 (twenty-sixth postoperative day). Except for some further decrease in the opacity at the upper part of the left thorax the condition is essentially the same as noted on the previous roentgenogram.

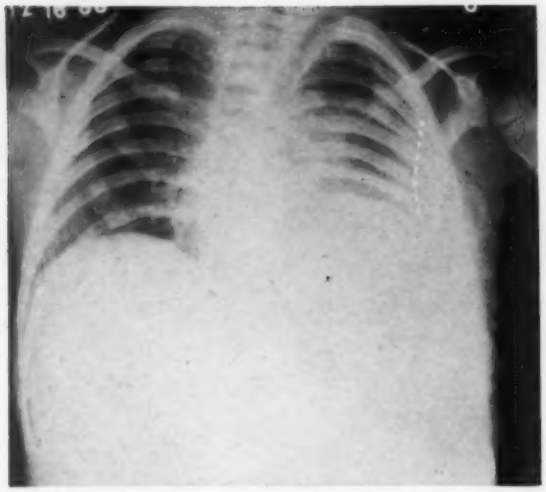

Fig. 14. Case 11. Roentgenogram taken on December 16, 1938 (thirty-third postoperative day and two days after the expectoration of mucoid material). The upper half of the lung field is somewhat less infiltrated than previously. However, the lower half does not show any appreciable change. The expansion of the lung remains the same as seen in Figures 11, 12 and 13.

(Fig. 12) failed to show any appreciable change from that of the previous two roentgenographic studies. The degree of expansion of the lung

Fig. 15. Case 11. Roentgenogram taken on December 20, 1938 (thirty-seventh postoperative day and six days after the expectoration of the mucoid substance). The upper part of the left lung field is clear. The lower part is slightly less dense. There is some expansion of the lung compared to that noted on the previous roentgenogram.

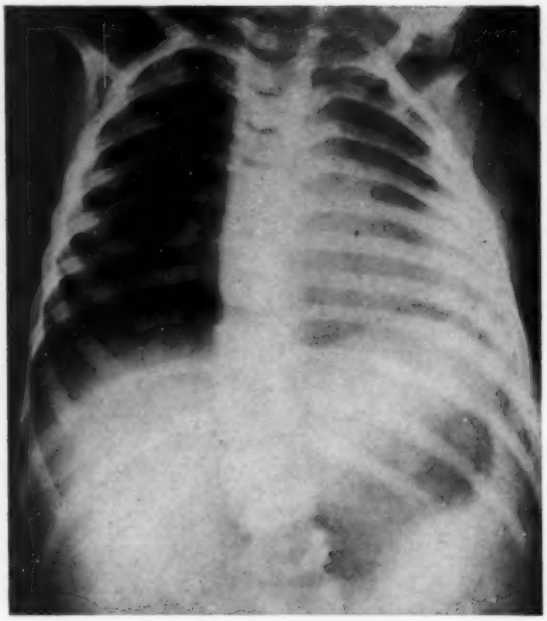

Fig. 16. Case 11. Roentgenogram taken on December 29, 1938 (forty-sixth postoperative day). The lung is almost completely expanded. There is some thickening of the pleura in the left axillary region.

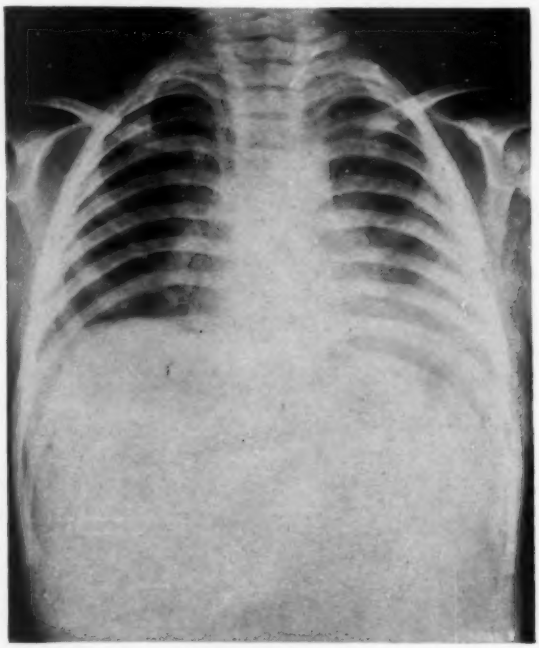

Fig. 17. Case 11. Roentgenogram taken on January 4, 1939 (day before discharge). The left lung is completely expanded. There is some thickening of the pleura in the axillary region. There is no apparent re-accumulation of fluid.

was unchanged, as was the infiltration of the lower half of the lung. Eight days later the patient's condition still continued poor. The patient appeared exhausted. A roentgenographic study of the chest at this time showed a slight decrease in the opacity of the upper half of the lung field (Fig. 13). However, there was no change in the pulmonary infiltration at the base of the lung, nor was there any change in the degree of pulmonary expansion. In spite of what was apparently adequate care and drainage, the temperature continued to be irregularly elevated. Five days later (Chart II, B) the patient was suddenly seized with a bout of coughing and expectorated a large quantity of thick blood-stained mucoid material. A roentgenogram of the chest two days later again showed no change in the infiltration of the lower left pulmonic field, nor was there any change in the degree of pulmonary expansion (Fig. 14). For the next three days the temperature continued irregularly elevated; drainage by way of the tube was less than previously but had not ceased. On the fourth day the temperature began to subside; the patient appeared remarkably better, although the roentgenogram showed only a slightly lesser degree of pulmonary collapse (Fig. 15). The pulmonary infiltration was still unchanged. Two days later the temperature declined to normal and remained so for the next two weeks, at which time he was discharged from the hospital. A roentgenogram made on the eighth day of normal temperature showed only a peripheral area of incompletely expanded lung (Fig 16). The day before discharge another roentgenogram was made (Fig. 17), which showed the left lung completely expanded and well aerated.

DISCUSSION

Coryllos and Birnbaum have shown experimentally that massive atelectasis and lobar pneumonia have a common pathogenesis and that both are secondary to bronchial obstruction. They believe that lobar pneumonia is a pneumococcus atelectasis due to bronchial obstruction by mucous exudate infected with virulent pneumococci. It has been shown frequently in experimental pneumonia, that the intra-alveolar exudate accompanying the early phases of pneumonia tends to coagulate during the "stage of red hepatization" and liquefy during the "stage of yellow hepatization." If the latter does not occur or is incomplete, the coagulum may remain in the lung and prevent aeration. Oertel has pointed out that in the stage of resolution of pneumonia, "the softening of the exudate and the restoration of the circulation corresponds with the crisis. It terminates the reaction of the body to the invader, but does not necessarily mean that the patient is going to get well. Very little of the exudate is expectorated; most of it is resorbed. . . . The first necessary step in resolution is the clearing of the lymphatics and blood vessels which occurs when the exudate is properly softened. If this does not take place, the exudate remains in the septa and gives rise to other difficulties." The retention of such secretions will therefore produce (or maintain) an atelectasis distal to the point of obstruction, thereby preventing aeration and expansion of the lung.

Peppard in 1927 presented 4 cases in which massive atelectasis was a postpneumonic complication. If we interpret these latter observations in the light of the foregoing, we can recognized the fact that various degrees of resorption are possible and that in Peppard's cases the resorption was minimal and/or there was obstruction to the bronchus. When, on the other hand, the resorption is incomplete, the patient is said to have "an unresolved pneumonia." This condition (which should better be termed "incompletely resolved pneumonia") is too well known to require much further comment. Suffice it to say that incomplete resorption of the exudate and therefore patchy atelectasis occurs in 2 to 3 per cent of all cases of lobar pneumonia.

Holinger subjected 3 patients with so-called "unresolved pneumonia" to bronchoscopic examination. He noted abundant purulent bronchial secretions with stenosis and inflammation of the bronchi leading to the collapsed lung. These observations would tend to corroborate the foregoing remarks on bronchial obstruction by retained secretions as a cause of incompletely resolved pneumonia.

The frequency with which empyema occurs during or after infections of the respiratory tree (particularly lobar pneumonia) is well known to every practitioner and need not be elaborated upon here. Empyema is said to occur in from 2.2 to 3.6 per cent of the cases of lobar pneumonia (Osler). The incidence of coexistence of incompletely resolved pneumonia (postpneumonic atelectasis) and empyema is therefore approximately 1 in every 1,500 cases of lobar pneumonia.

Another factor which operated to enhance the atelectasis is compression of the lung by the intrapleural exudate (empyema). This pressure and the bronchial obstruction impair the circulation within the collapsed lung and thus inhibit resorption of the exudate. Coryllos and Birnbaum have shown that in the compressed, atelectatic (apneumonic), collapsed and consolidated lung the capillary circulation is diminished proportionately to the degree of shrinkage of the lung. They observed that circulation and ventilation of the lung are parallel functions, and that when one is diminished the other is proportionately decreased. Thus, in the atelectatic lung the flow of blood in the capillaries is progressively impaired. In the first case reported by Butler, that of a man, aged seventy, who developed a postpneumonic atelectasis and empyema, there was a suspicion of an underlying cancer of the lung as the cause of the atypical postoperative course. An exploratory thoracotomy was performed. It was noted that when the collapsed lung was incised it was avascular—further proving impairment of circulation in the atelectatic lung.

In the 5 cases reported by Butler* and the 2 presented in this paper, the patients' age ranged from three to seventy years. In 4 cases it followed lobar pneumonia of the left lung, and in 3 it followed a similar process on the right. Bacteriologic studies of the pleural exudate in 5 cases showed pneumococci in 2, pneumococci and streptococci in 2, and *Streptococcus viridans* in one. In all 7 cases the empyema was treated by preliminary aspiration followed by rib resection drainage. The postoperative convalescence in all 7 cases was poor. After the initial drop in temperature which followed surgical intervention for the empyema, there was a secondary rise, usually taking place during the latter part of the first postoperative week. In some instances the temperature rose steadily to 102° F. In the 2 cases presented in this article, postoperative roentgenographic studies of the chest showed incomplete expansion of the lung, infiltration of the affected lung, and a residual collection in the pleural cavity. Serial roentgenograms over a period of weeks failed to show any progress in the degree of pulmonary expansion after the initial, immediate, postoperative expansion. Four of the cases reported by Butler were subjected to bronchoscopic examination. In these cases there was narrowing and inflammation of the bronchial wall, but no retained bronchial secretion could be observed. The 2 cases reported here were not bronchoscoped. In the former 4 cases and the latter 2 cases there was rapid and progressive improvement after bronchoscopic manipulation or expectoration of the thick blood-streaked mucus. In all of these cases the patients felt considerably better after this had taken place—they were able to breathe more easily, the temperature began to fall, and the lung began to expand soon thereafter.

Postoperative atelectasis, involving as much pulmonary parenchyma as is encountered in the cases of empyema with postpneumonic atelectasis, is usually associated with crowding the hemithorax by the retraction of the mediastinum, elevation of the diaphragm, and contraction of the intercostal spaces on the affected side. These changes are the result of the increased negative intrapleural pressure resulting from the occlusion of the bronchus and col-

* In one of these cases, which terminated fatally, there was found at necropsy a healing lung abscess in the right lower lobe, an atelectasis of the right middle lobe, an acute pneumonia of the left lung, and a pleural effusion on the left. As Butler suggests, this case may be eliminated from consideration because the atelectasis found at necropsy probably did not modify the clinical course.

lapse of the lung. The more highly negative this pressure becomes, the greater is the degree of shrinkage of the hemithorax. Because of the altered intrathoracic status (postpneumonic infiltration of the lung, empyema, surgical opening into the pleural cavity, and the presence of some degree of pneumothorax), the changes accompanying postoperative atelectasis are not elicited in these cases. The mediastinum, diaphragm, intercostal spaces, etc., are altered in position and configuration only so far as they are affected by the resultant forces of the newly created intrathoracic status and intrapleural pressure. The uniform course in all of these cases warrants the observation that in any case of postpneumonic empyema which assumes an atypical course and which is associated with incomplete expansion of the lung, the presumptive diagnosis should be bronchial obstruction until it is ruled out. In the light of the bronchoscopic observations in such cases it appears that the persistent atelectasis after adequate drainage of the purulent collection can be attributed to retained secretions in the smaller radicles of the bronchial tree—in the bronchioles and alveoli.

CONCLUSIONS

The failure of the lung to expand following surgical drainage of postpneumonic empyema may be due to bronchial obstruction caused by retained secretions. The etiological agent in the genesis of such atelectasis is apparently the presence of thick mucus in the smaller bronchioles and alveoli. Roentgenographic studies are indispensable in the diagnosis. If the obstruction is not relieved it leads to chronicity; when relieved early it leads to rapid and complete expansion of the lung and cure of the empyema.

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CRANIAL OSTEOMAS

FROM A ROENTGENOLOGIC VIEWPOINT

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WHAT is an osteoma? The answer to this question is not as simple as it may seem. The dictionary (Standard) states that an osteoma is a bony tumor, a hard tumor of bone-like structure developing on a bone and sometimes on other structures. But it must be borne in mind that there are many forms of bone hypertrophy (tumefaction) which are not osteomas, such as the overgrowth associated with reparative reactions, from infections, invasive tumors, and other forms of irritation. Hence we shall have to be content to state that a true osteoma is a bony tumor which exhibits neoplastic characteristics, but not all bony tumors are osteomas. Ewing states that even the microscope at times fails to differentiate osteomas from simple bony hypertrophy. So we see that our original question cannot be answered satisfactorily until we learn more about the origin of these interesting tumors. Ewing describes the bony tissue forming an osteoma as ivory-like with solid lamellae and with few or no haversian canals, or it may be spongy with cancellous tissue, or it may contain marrow cavities or spaces. Thus it can readily be seen that merely because the tumor does not appear dense in the roentgenogram it is not necessarily an osteochondroma, but may be an osteoma with less dense spaces scattered throughout its mass. The less densely formed osteomas will usually be found arising from cartilage or bone of cartilaginous origin, while the dense tumors as a rule originate from bone of membranous origin, from periosteum, or within the bone itself.

When osteomas occur in the skull they will usually originate in certain sites of election. One of the most common locations for these tumors is in the fronto-ethmoidal region, and less common locations are in the middle fossa and involving the petrous pyramids.

The group of osteomas used for this review consisted of 48 cases, and of these 60 per cent were fronto-ethmoidal in origin divided nearly equally between an origin wholly within the frontal sinuses and an origin involving the vertical portion of the frontal bone. Thirteen per cent were found to originate in the orbito-ethmoidal region which, generally speaking, could be classed as frontal. Another 13 per cent originated in the parietal bones. Six per cent were found involving the petrous portions of the temporal bones, while tumors arising from the squamous portions of the temporal bones accounted for 4 per cent of the total number. Another 4 per cent were found in the occipital region. It might be of interest to quote here Fetissof's figures based on a total of over 200 cases, showing the distribution of osteomas in the nasal accessory sinuses. He found 50.7 per cent of the total number situated in the frontals, 26.7 per cent in the ethmoid labyrinth, 6.2 per cent in the maxillary sinuses, and 3.1 per cent in the sphenoid sinuses.

Usually osteomas will be found arising from the surface of the bone and can therefore be designated as exostotic, but not infrequently their origin will be seen to be enostotic or within the bone. Fetissof is of the opinion than an osteoma grows from within, due to a metaplasia of fibrous tissue directly into bone. It should be noted that osteomas and fibromas have many points in common, but the osteomas have true bony capsules. As a rule, the osteomas occurring in the frontal region and those involving the facial bones will be of the enostotic variety. This is likewise true of the osteoma found involving one or more of the bones forming the vault. These calvarial osteomas usually originate in the diploe and involve one or both of the adjacent tables.

The etiology of the osteomas is as obscure as the etiology of other forms of neoplasms. Arnold thinks they arise from cartilaginous or periosteal embryonal rests. He points out that their usual sites of election are where two forms of bone are joined. Fetissof presents considerable evidence to support his theory of a periosteal origin. Kretschmann suggested in 1910 that the sutures in the skull might be likened to the epiphyses in the long bones, and as many cranial osteomas occur near suture lines the similarity of origin with such tumors found elsewhere becomes obvious, but he offers no definite theory as to etiology. After considering the various theories regarding the origin of these tumors, we are forced to conclude that the answer has not yet been found. It is interesting to note that there is considerable evidence to support the theory that trauma or infection may at times stimulate an osteoma to speed up its ordinarily very slow growth. Most of the evidence, however, seems to indicate that a year or two may intervene between the trauma and any appreciable increase in size of the tumor. If an injury can actually cause such a tumor to grow, then we might go a step further and consider trauma, or any source of irritation, as a possible stimulus to the original anlage, whatever that may consist of, and so start such a tumor on its course.

A perusal of the literature elicits the interesting fact that cranial osteomas are more prevalent in males than in females. This observation is difficult to explain unless it is because more male skulls have been examined, due chiefly to the greater prevalence of trauma to men. Most osteomas originate in young people and rarely do we find such tumors beginning in persons past middle life.

Intracranial and especially frontal osteomas are not infrequently associated with mucoceles. This is a condition which was most interestingly and dramatically described and discussed by Cushing. When such an association occurs, the growth is apt to extend intracranially far enough to puncture a lateral ventricle, and the only known way to stop such progress is by operation. If a ventricle is invaded in such a manner we will usually find that an autopneumo-encephalogram has been produced which may outline the extent of the invasion. Occasionally a tumor may break through the inner wall of the frontal or ethmoidal sinuses and so permit air to reach the subdural or subarachnoidal spaces, and cases have been reported where the cerebral substance was invaded so that a pneumatocele was produced, which might be termed a pneumo-encephalocyst. Osteomas may invade the orbits, neither orbit being more prone to involvement than the other, but when an orbit is involved there is usually some exophthalmos of a nonpulsating type, and not infrequently the patient will complain of double vision, with or without an actual displacement of the eyeball, usually downward and outward if present. Such orbital tumors are chiefly ethmoidal in origin and occasionally they will be pedunculated. The orbitoethmoidal tumors may at times extend backward and appear in the roentgenogram in a manner strongly simulating an olfactory groove meningioma, and such a finding may be so striking as to make a

Fig. 1. A flat osteoma of the left temporal bone.

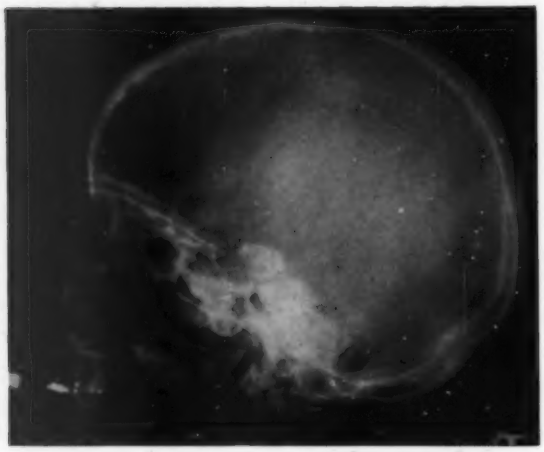

Fig. 2. A small osteoma situated near the outer tip of the petrous pyramid.

differentiation very difficult. Usually, however, in good stereoscopic films it will be possible to trace the bony growth to the inner orbito-ethmoidal region, and as Cushing has pointed out, most meningiomas, with which such a tumor might be confused, originate from the outer third of the sphenoid ridge, hence a differentiation is usually possible. It would be well to have the history of the case, and if possible, the clinical findings readily available when attempting to evaluate such changes seen in the roentgenogram. Usually the symptoms would be of greater severity in the presence of an olfactory groove meningioma than with a relatively small osteoma.

A few authors writing on the subject of cranial osteomas seem to feel that all such tumors are progressive, and unless surgically treated the prognosis will invariably be poor. Cumston, however, has had the opportunity to check up on cases which have harbored such tumors for many years, one as long as forty-two years, without showing serious complications. Certainly a fairly large proportion of the osteomas we find incidentally in an examination for other suspected pathology are growing at an extremely slow rate, if at all. Such a tumor, however, must always be considered as a potential source of trouble, particularly if the patient harboring it should be subjected to trauma which may stimulate its propensities for growth. The endocrine status of the patient may influence the tendency of the tumor to grow. A case with hyperpituitary tendencies might well be checked up more frequently than one not so constituted.

Many cranial osteomas are asymptomatic. This is particularly true of the tumors found in the frontal sinuses. If they are too small to produce pressure on adjacent sinus walls or block a sinus outlet or produce pressure on a sensory nerve, their discovery would be purely accidental and incidental. The osteomas involving the outer walls of the frontal sinuses are less apt to become of clinical importance than those situated elsewhere. If we discover the presence of an asymptomatic osteoma it would be wise to re-examine the patient at least every six or eight months in order to check on the size of the tumor. If it shows any increase in size it should be removed. It might not be out of place to mention in connection with such comparative examinations that the technique employed in obtaining the films must be closely comparable. This can be checked by measuring the overall diameters of the skull in the two sets of films, and if any appreciable variation exists, a proportionate variation must be allowed when measuring the size of the tumor shadows. Such allowances would compensate for variations in target film distances, but presupposes similar positioning and closely similar film densities. Many mistakes have been made, and are still being made, by attempts to compare noncomparable sets of films. If the tumor shows signs of enlarging, it certainly should be removed. It might be of interest to note here that in 1864 an attempt was made to remove an osteoma from a patient in the Massachusetts General Hospital of Boston. If this was not the first, then it must have been nearly the first such attempt to be made in this country.

When considering the interval which might safely be allowed to elapse between check-up examinations, it should be borne in mind that osteomas are apt to grow more

rapidly in young people and that the spongious type of tumor will enlarge more rapidly than one composed of dense sclerosing bone. Incidentally, the sclerosing type of tumor may be broken off surgically, or may even slough off, and it is not likely to recur, but, on the other hand, a successful removal of a spongious osteoma necessitates a careful and complete removal of the tumor together with some of the adjacent and underlying normal bone.

There are several conditions occasionally encountered in examination of skulls which are somewhat difficult to classify without reservations as true osteomata. The first of these conditions that we will discuss is an hypertrophy of bone occurring at the intermaxillary and palatomaxillary suture. Such a bony overgrowth is known as a torus palatinus.

This interesting anomaly is usually in the form of two bony nubbins situated one on either side of the suture. Frequently these nubbins are very small, or they may reach a diameter of several millimeters. Their discovery, as a rule, is incidental, and by some they are considered as familial or even racial characteristics. The races inhabiting the temperate and torrid zones are more apt to possess such bony tubercles than those living in the more rugged climes. But interestingly enough, people living in the northern countries occasionally exhibit a somewhat similar pair of bony knobs known as torus mandibularis. These are found at about the level of the second premolar teeth and about 1 cm. from the alveolar margin. Occasionally both a torus palatinus and mandibularis will occur in the same individual.

The torus palatinus and torus mandibularis are evidently genetic in origin and therefore not osteomas, but on rare occasions we will find these nodules enlarged, particularly the torus palatinus. It is under such circumstances that we might be justified in considering the possibility of the presence of a superimposed osteoma. This is especially true if we find a concomitant bony tumefaction extending

Fig. 3. An osteoma of the frontal bone. The frontoethmoidal region is a common site of election for these tumors.

along the intermaxillary suture. It is undoubtedly true that histologically these bony tumors are indistinguishable from the osteomas, but etiologically they are evidently congenital in origin and therefore their growth, if any, is to be explained on some as yet rather obscure endocrine basis.

There would be no great importance attached to the finding of either form of torus or bony hypertrophy along the intermaxillary suture, unless the hypertrophy could be demonstrated to be enlarging, or by its presence the overlying soft tissues were being subjected to an abnormal amount of trauma, or that there might be some interference with contemplated maneuvers of a dental surgeon.

Occasionally we find plaques of calcification in the meninges which have progressed to actual ossification in whole or in part. Such ossification might well be classified as at least osteomatoid if not as a true osteoma. They are evidently formed by a metaplasia of fibrous tissue directly into bone. Such osteoidomas are not infrequently found in the falx cerebri, and they are usually roughly triangular in shape with

Fig. 4. An osteoma of the petrous portion of the temporal bone. It is of the combined dense and spongy type.

the base in the falx. In well made films of sufficient density to show bone detail, such deposits can usually be differentiated from the more commonly found calcific deposits. These osteoidomas of the falx are supposed to be asymptomatic, but when one attains a considerable size it seems highly probable that it may become at least a potential source of irritation to the adjacent surfaces of the cerebral hemispheres.

The dura may be found to be involved in a bony metamorphosis. When such a condition is recognized its status should be checked every few months, and if it is seen to be enlarging with any rapidity, one would be justified in suspecting the presence of either an osteoblastic or an "en plaque" type of meningioma, even though the overlying inner table of the calvarium be uninvolved. Any enlarging tumor mass, whether due to a simple fibro-osseous metaplasia or to something else such as a meningioma, should receive careful surgical consideration, because in either case the tumor becomes simply an accident awaiting the opportunity to happen.

Ossification occasionally will be found in the presence of an old hematoma. Such ossification will usually be quite irregular, and in addition will be complicated by irregular deposits of calcium which would be predominant. In good stereoscopic films the entire involved area will be seen to be very irregular in outline and thickness. The calcium and osteoid deposits will not be confined to the meninges but will be seen scattered throughout the mass. If the hematoma be of the "en plaque" type then the deposits will appear to be in one plane, but the extreme irregularity and confluency of the osseocalcific deposits would lead one to suspect a hematoma rather than the more benign forms of meningeal osteoidomas. The history and clinical findings must always be seriously considered when attempting to make a differential diagnosis. Dyke and Davidoff pointed out that in the presence of a chronic hematoma we may find a depression of the floor of the cranial fossa in which the mass exists as compared to the opposite side. This finding is more common in the middle fossae. The osteoid changes, however, are much more commonly found in lesions over the convexities which would not be expected to influence materially the bones of the base.

Not infrequently we encounter rather widespread osteohyperplasias in the skull and it is rather difficult to draw the line between "simple" hyperplasias and true osteomas. Certainly the condition known as general hypercraniosis which consists of a general thickening of the bones, chiefly the vault, but without undue increase in density or porosity, is not to be considered related to a diffuse osteoma. Nor is the condition called by Moore hyperostosis frontalis interna, an osteoma, although at times the bony hypertrophy might closely simulate an osteoma. These bony overgrowths are evidently due to a basic metabolic disturbance probably endocrinopathic in origin. There is still another diffuse bony hypertrophy that is not so easily disposed of, which goes by the name of leontiasis ossea. It is a diffuse hyperostosis of dense sclerotic bone usually involving

the bones of the face and often spreading to the frontal region. This strange bony overgrowth has also been known as creeping periostitis of the bones of the face and skull.

Leontiasis ossea is not easily placed in the catalogue of diseases. Attempts have been made to associate it with Paget's disease, but without much success. It has been thought of as a disease entity, and by some it is still so considered. Perlberg and Kruger recently reported a case which they considered a diffuse osteoma. Strangely enough this same case was studied in our clinic fifteen years ago. A comparison of the extent of the condition seen in Figure 5, with the illustrations of the same case reported by Perlberg and Kruger, will seem to indicate that the condition progressed to a certain point and has for years remained practically unchanged. This would be compatible with the observed characteristics of a fairly diffuse osteoma of sclerotic type, but in this case the dense bony overgrowth occurred in a relatively short time which is not characteristic of the sclerotic type of osteoma.

Fig. 5. Leontiasis ossea. Note the distribution of the thickened bone and its extreme density. The changes are confined chiefly to the frontal, basal, and facial bones.

Fig. 6. Leontiasis ossea. Same case as Figure 5, posteroanterior view.

Hamburger and Nachlas in 1926 reported finding leontiasis ossea in a case suffering with well marked Paget's disease, and concluded the two conditions were the same etiologically. But as we find these two diseases separately more often than together, it seems more likely that they are separate entities. In 1929, Ruppé reported 5 cases of leontiasis ossea and in one he found the condition to have involved the two upper cervical vertebrae. Such a finding is rather remarkable and would be very significant if other similar cases could be discovered, for if it could be definitely demonstrated that the condition is not localized, then we might be justified in concluding that it is not a simple diffuse osteoma.

It may be that leontiasis ossea is simply an atypical diffuse osteoma, and as we cannot very clearly define an osteoma it would be difficult for anyone to say definitely that

it is not. But as the hypertrophic bone itself and its distribution, involving as it does several bones simultaneously, does not readily fit into the category of any of our better known bone diseases, it would seem better, at least for the present, to consider leontiasis ossea as a disease entity, or perhaps a form of melorheostosis.

To recognize an osteoma in the roentgenogram is usually not difficult, but one should be careful not to be too hasty in calling an area of bony overgrowth seen in the skull an osteoma until all other possibilities have been carefully considered, chiefly because the osteomas constitute only about 1 per cent of all cranial new growths. The osteomas we see in the calvarium are apt to be rather flat. They usually do not show any evidence of bone destruction, both inner and outer tables are likely to be involved, and if any vessel channels can be seen passing over the tumor they will usually appear smaller in the portion directly over the mass. This is in contradistinction to the hypervascularity one might expect to find if the hypertrophy were due to a meningioma. The spongy type of tumor may destroy the underlying or adjacent bone, so that we not infrequently see areas of decreased density about the base of the tumor.

We often find small areas of increased density in the bones of the vault. These areas are due to localized bony condensation due to anomalies of growth and development. The bone within these areas will be seen to be of normal structure but of greater density than the surrounding bone. There will be no tumefaction and no alteration in size or course of any vessel channels in the vicinity. These areas are not osteomas, but occasionally their appearance may prove sufficiently dense to be somewhat confusing.

Any bony hypertrophy seen in the nasal accessory sinuses or involving the bones of the face might well be considered an osteoma until proved otherwise. There are also small bony nodules sometimes seen in the external auditory canals. These are probably congenital and are rarely recognized in the roentgenogram. Occasionally however, they may enlarge and take on some of the characteristics of a new growth, and might therefore be considered as at least potential osteomas.

Searching for an osteoma is somewhat like the proverbial chase of the "will-o'-the-wisp," for in either case we are not quite sure just what it is we are after; but even so it is well worth while to carefully note the presence of these bony growths because they may and often do become a definite clinical problem.

SUMMARY

The osteomas of the head have been discussed and an attempt made to define them. Several allied conditions have also been discussed and their relationship to or independence of the osteomas considered.*

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Vol. 44, No. 2

OSTEOPETROSIS

REPORT OF A CASE

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THE condition now known as osteopetrosis was mentioned in association with leukemia and pseudoleukemia as early as 1879 by Hueck, 1880 by Neumann, and 1901 by v. Jaksch. A roentgenologist, Albers-Schönberg, first described the condition roentgenologically in 1904, and it has been known since that time by his name, or the name "marble bones" which he used in the description of the picture. Karshner, in 1926, collected 18 cases from the literature and added four of his own. McCune and Bradley, in 1934, found 69 cases. Wortis, in 1936, added one case and stated that less than 80 cases were on record. Nussey, in 1938, tabulated 112 cases. Since the latter tabulation reports have appeared by Clifton, Frank, and Freeman,[5] Lamb and Jackson,[12] Anderson,[3] Gerstel,[6] and Langston.[13] The case to be reported, then, is the one hundred and eighteenth.

CASE REPORT

The patient is a white female, aged thirty, who was first seen in the Out Patient Department of the University of Oregon Medical School in October, 1938. Her chief complaints were blindness, pains and aches in the muscles, anemia, and headache. She admitted that she had never been well, and that she had had impaired vision since her earliest recollection.

She is the third of five children, all the other siblings being free of the patient's complaints. There is no history in the family, immediate or remote, of any similar trouble, so far as she is aware. There was no blood relationship between the parents. They came from widely separated areas of Switzerland. The father died at the age of seventy-two of kidney disease. The mother died at the age of thirty-five following childbirth.

As far as can be ascertained, the mother was well during her pregnancy with the patient, the birth at full term and spontaneous. She is uninformed of her developmental history, except that she is quite positive that she had two teeth at birth, and that her permanent dentition did not come until she was eighteen years old. In her infancy, she vomited whenever she drank milk although she has no such difficulty at present. During this time she was taken to doctors many times because of rickets. At the age of two she did not respond to greeting such as waving of the hand. She believes this to be her first intimation of impaired vision. She became certain of her inability to see normally at the age of six because she could see nothing when the left eye was covered or closed. Between the ages of six and seventeen she suffered six or seven fractures in the extremities from apparently trivial causes, although she took part in more strenuous activities with her playmates without any mishap. Tonsils and adenoids were removed in childhood. She had pertussis, measles, and mumps as a child.

She feels sleepy during the day, and has frequent headaches but no dizziness. Her teeth have always been troublesome. In the last two years she has had some thirty cavities with difficulty in retaining the corrective work. Her gums bleed easily, but no teeth have fallen out. The menarche occurred at eighteen years of age, regular, with a scanty flow of three days. At the present time, the flow is almost negligible although there is a regular period.

She is cooperative and intelligent. She went to the eighth grade of grammar school, with the aid of a magnifying glass, but finally had to leave because of the failing vision. At the present time she is studying braille because she fears imminent total blindness.

Physical Examination. The patient is a small, pale individual weighing 103 pounds, and measuring 60 inches in height. The pulse is 120, and the blood pressure 125 systolic, 85 diastolic. The pupils react to light and accommodation. The extra-ocular muscles are intact and there is no nystagmus. Examination of the fundi reveals a striking bluish pallor of the discs bilaterally. The nose, hair, skin, tongue and

Fig. 1

pharynx reveal no abnormality. The palatal and gag reflexes are present and normal. The thyroid is not palpably enlarged, and there are no pulsations or glands palpable in the neck. The chest is pidgeon shaped but there is no rachitic rosary or Harrison groove. The breasts are atrophic. The heart is normal in size, the rhythm regular and action rapid. No murmur is heard or thrill palpable. The lungs and abdomen are normal. Neither the liver nor spleen is palpable. The tendon and skin reflexes are normal. Vibration sense is intact. Sensory examination reveals no abnormalities. Both humeri seem to be short in relation to the rest of the arm, and there is limitation of motion in the right hip joint.

Fig. 2

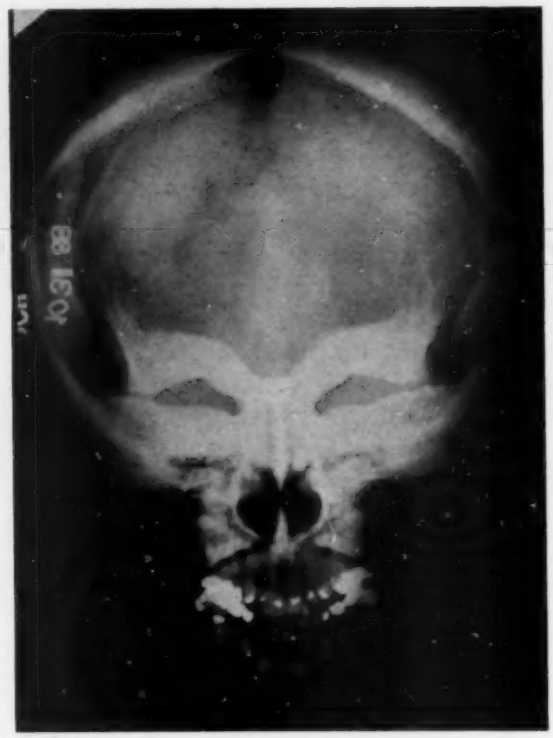

Fig. 3

Laboratory Examination.

Urine: pale, cloudy, specific gravity 1.010, no abnormal findings.

Hematology	*October, 1938*	*March, 1939* After iron therapy
Hb	67.1%	80%
Red blood cells	3,070,000	3,960,000
Color index	1.06	0.97
White blood cells	8,250	7,600
Polymorphonuclears	75%	72%
Eosinophiles	2%	
Small lymphocytes	14%	25%
Mononuclears	2%	1%
St. cells	6%	2%
Platelets		268,000
Sedimentation rate	3/22 per 15/45 min.	4/30 per 15/45 min.

Blood Chemistry	
Calcium	10.9 mg. per 100 cc.
Phosphates	3.9 mg. per 100 cc.
Dextrose	91.0 mg. per 100 cc.
Cholesterol (whole blood)	176.0 mg. per 100 cc.
Protein	6.6 normal albumin-globulin ratio

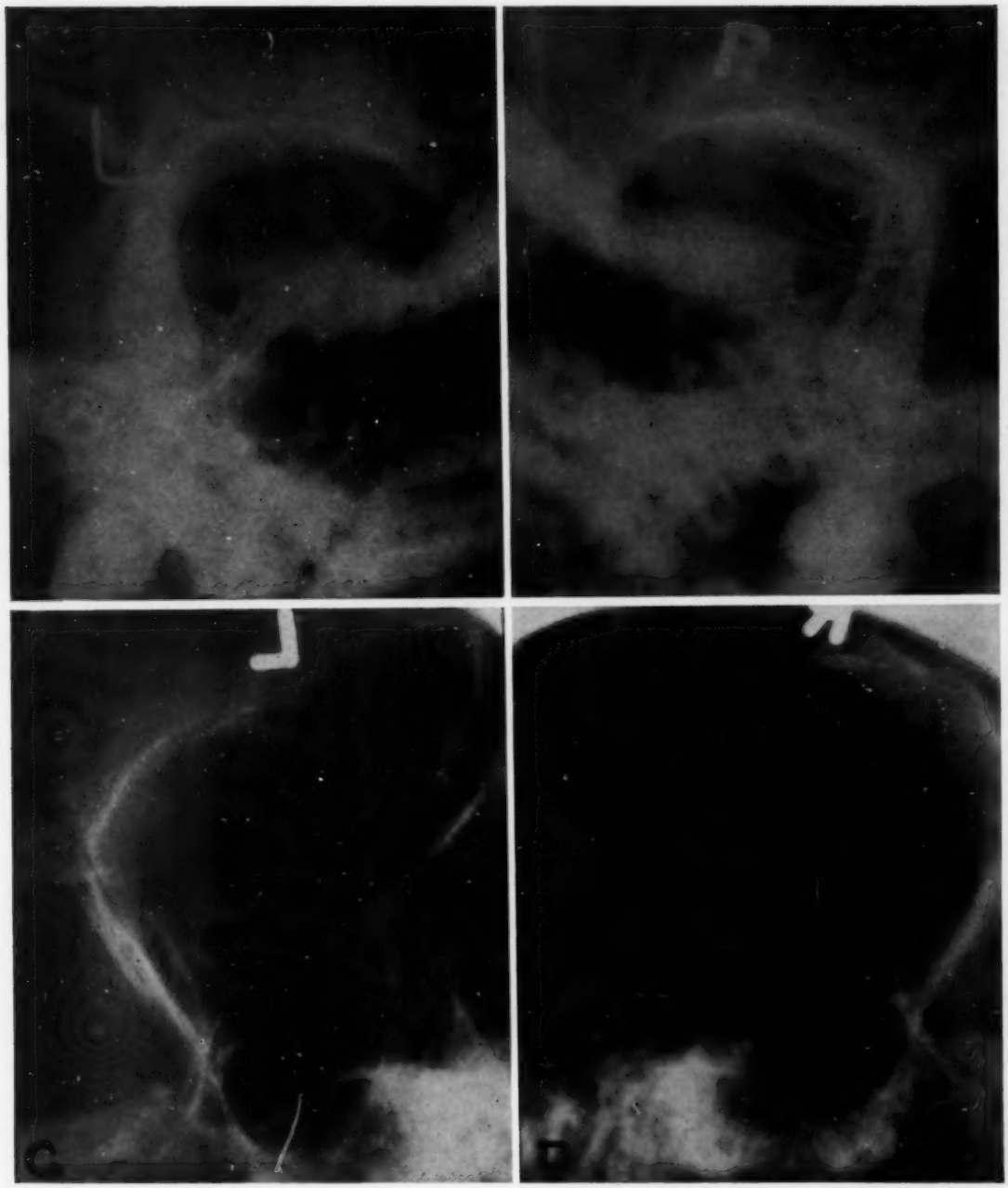

Fig. 4

A basal metabolic determination is −7 per cent. The electrocardiogram shows a right axis deviation.

Roentgenologic Appearance. Films of the pelvis and skull were first made and the spectacular appearance shown in Figures 1 and 2 was seen. The entire skeleton was then roentgenographed and the peculiar dense bone change, characteristic of osteopetrosis, was found in all the bones except those of the face. In the skull, the most severe involvement is at the base, especially in the sphenoid bone (Figs. 2 and 3). This bone stands out in all roentgenograms as if it had been specially prepared with an opaque medium. The greater and lesser wings are very distinct. The sella turcica is about normal size but the anterior and posterior clinoids are dense and thick. The temporal bone is also involved,

Fig. 5

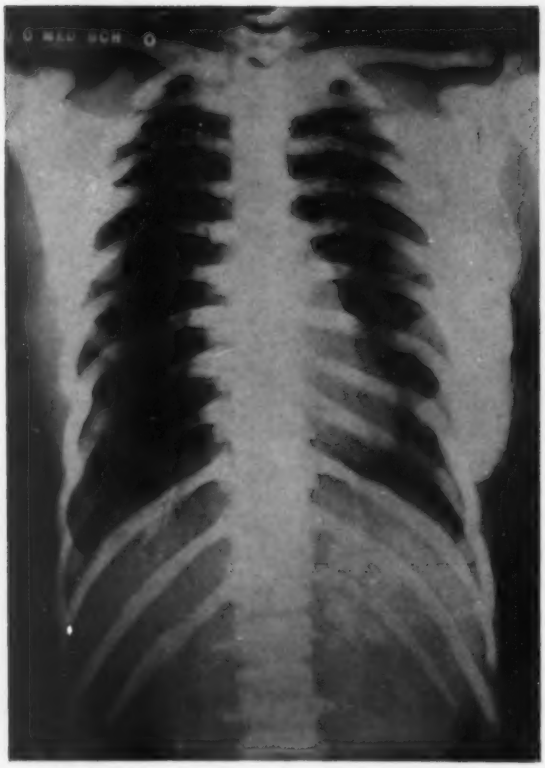

Fig. 6

the mastoid regions, the petrous portions and the squama being much more dense than normal. The styloid processes are elongated and prominent due to their increased density. It is interesting that the bones of the face escape involvement almost entirely. The mandible and the maxilla are approximately normal, and the development of the teeth is unimpaired despite the patient's dental troubles.

The spine presents essentially the same picture from the cervical region to the sacrum

Fig. 7

(Fig. 5). The most dense portions of the vertebral bodies are those adjacent to the intervertebral discs. The central cancellous portion appears almost normal. The vertebral appendages are uniformly involved, the lamina being the most dense and the spinous and transverse processes slightly less prominent. The ribs (Fig. 7) are uniformly dense from the vertebral to the sternal end, with complete disappearance of the cancellous structure. Several old fractures are noted, especially in the lower ribs.

In the shoulder girdle, the clavicle shows a narrowing of the medullary canal with a marked increase in the thickness of the cortex (Fig. 6). The scapula shows a major involvement around

the glenoid. The characteristic density and narrowing of the marrow cavity is found in the humerus and the bones of the forearm. This condition is very marked in the bones of the lower extremities (Fig. 7). The carpal bones show concentric rings of increased density with a small layer of normal bone just beneath the cortex, and a small central area of normal bone. The metacarpals and phalanges show most marked changes in the diaphyseal portion with the head and base of each bone quite normal. A similar situation is found in the tarsal and metatarsal bones.

The pelvis presents spectacular changes (Fig. 1). Both ilia show crescentic layers of dense bone laid down over the crests presumably as the bone grew. The femoral heads and upper shafts are on each side extremely dense and are the seat of old pathological fractures. Very little evidence of normal bone structure is seen in this part of the skeleton.

The optic foramina have been shown at autopsy, in a few cases, to be narrowed significantly (Lorey and Reye,[14] Kraus and Walter,[11] Alter, *et al.*[2]), but according to McCune and Bradley[15] attempts to demonstrate this narrowing during life have been unsuccessful. We have succeeded in demonstrating roentgenologically the encroachment upon the optic foramina by the bony change (Fig. 4*A* and *B*). It can be seen by comparing with a normal optic foramen (Fig. 4*C* and *D*) that the foramina are definitely narrowed and that the outlines are not clear cut. Furthermore, the changes are greater on the right side where eyesight is entirely gone. Clegg[4] stated that the average normal measurements for the optic foramen are 4.1 by 4.65 mm. with no variation due to age, sex or stock. He also stated that if the canal measures less than 2.8 mm. in any one of its diameters it cannot contain a normal optic nerve. The measurements of the greatest diameter of the optic foramina in this case are 2.8 mm. on the right and 3 mm. on the left.

DISCUSSION

From a clinical standpoint, this case is fairly typical. The symptoms associated with osteopetrosis are manifestations of the encroachment of the bones of the skeleton on surrounding organs. However, the degree of density does not always parallel the symptomatology. The diagnosis was first suspected in this case because of the presence of optic atrophy, anemia, and the history of multiple fractures. The optic atrophy especially is a constant finding in these cases. The anemia is usually present and may vary, most cases being of the hypochromic type, but a hyperchromic anemia has been reported in association with the picture. It is interesting to note that our patient responded to iron therapy with an increase in hemoglobin and red corpuscles.

The retarded development of the teeth, and the presence of marked cavitation in spite of much repair is typical. She has not, however, had any mandibular pathology which is reported in many other cases. It is possible that the late onset of the menarche and the present scantiness of menstrual flow may be manifestations of the encroachment of bone on the pituitary body. Our case is also typical in the subjective complaints of pains in the extremities and chest.

Our case differs from most reported cases in that there is no familial incidence nor was there any consanguinity in the parents. We cannot correlate the story of the presence of two teeth at the time of birth with the syndrome. The blood chemistry and metabolic tests are normal.

Roentgenologically, this case shows features found in some of the reported cases. However, since the degree of involvement varies markedly, not all the findings are present in our case. The ruffle-like appearance mentioned by Clifton, Frank and Freeman[5] as being so prominent in the long bones is not found except in the wings of the ilium. The involvement of the carpals, metacarpals, tarsals, metatarsals, and phalanges is similar in our case to that found in the case reported by Hodges, Phemister, and Brunschwig,[7] but in the present case the long bones of the upper and lower extremity are diffusely involved from one joint surface to the other, rather than in the central portion of the diaphysis alone. In the skull the involvement is most marked in the bones preformed in cartilage, as in the other reported cases. There is little involvement of the membranous bones of the skull. Epiphyseal development and

growth of bone appears to have been normal in this case, with the sclerosis developing after the primary centers of ossification were quite well developed, or else not affecting the ossification of the bones. It is interesting to note that the patient had several pathological fractures of which she was unaware.

SUMMARY

1. A case of osteopetrosis, diagnosed clinically, is reported.

2. The case shows many findings which have already been reported.

3. This case is interesting from the standpoint of the lack of familial incidence, the absence of consanguinity of the parents, the response of the hematology to iron therapy, and the demonstration of changes in the optic foramina resulting in optic atrophy.

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Vol. 44, No. 2

COMPARISON OF ROENTGENOGRAPHY AND DUODENAL DRAINAGE IN THE DIAGNOSIS OF CHOLELITHIASIS*

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THE rôle of the roentgenologist as a consultant makes it necessary not only that he be skillful in the field of roentgenology but also that he be familiar with other diagnostic procedures. This thought is well expressed by Kornblum and Tumen.[1] They state that "A working knowledge of the clinical significance of the various laboratory tests, both new and old, is of inestimable value to the radiologist." "Furthermore, intelligent roentgen interpretation is dependent upon a full appreciation of the significance of the clinical and laboratory data available in any given case. Only after careful correlation of the clinical, laboratory and roentgenological findings can an intelligent opinion be expressed regarding the significance of the roentgen changes."

Frequently in conference the roentgenologist is asked concerning the relative value of other methods of diagnosis as compared with roentgen diagnosis. Of special interest is the question concerning the merits of roentgenography and duodenal drainage in the diagnosis of cholelithiasis. When primary films and cholecystograms result in normal findings in the presence of positive clinical signs, the referring physician often confronts the roentgenologist with this question: "Do you think that duodenal drainage might help to corroborate the diagnosis inasmuch as the roentgen examination failed to do so?" In order to offer a satisfactory and accurate reply to this query we determined to evaluate the two methods, which is the subject of this presentation. The diagnosis of cholelithiasis in typical cases is rarely difficult by means of clinical history, physical examination, roentgenological and laboratory procedures. In atypical cases, however, the diagnosis may offer many pitfalls. The two most valuable procedures, in addition to clinical history and physical examination, are roentgenography and examination of the duodenal contents obtained by duodenal drainage.

This contribution consists of 54 cases which were studied by means of roentgen examination and duodenal drainage to determine the presence or absence of gallstones. All these cases were verified by surgical exploration and pathological examination. The tests were applied in some patients suffering from other diseases, such as carcinoma of the stomach, carcinoma of the liver, peptic ulcer, pancreatitis, and postoperative adhesions.

Cholecystographic examinations were conducted by the oral method, the dye, tetraiodophenolphthalein, being administered in 4 gm. doses. It is scarcely necessary to emphasize the importance of proper preparation of the patient and meticulous standardized technique in gallbladder roentgenography.

Duodenal drainage was conducted according to the method of Lyon.[2] This procedure is relatively simple in experienced hands. It consists of intubation of the duodenum under roentgenoscopic control in the fasting patient. This is followed by the installation of 90 cc. of a 30 per cent magnesium sulphate solution through the tube. Magnesium sulphate, when so introduced into the duodenum, according to the theory of Meltzer,[3] relaxes the sphincter of Oddi and induces emptying of the gallbladder. In the normal individual the bile will separate into three layers in the collecting bottle. The middle, or dark layer of "B" bile is the fraction studied for diagnostic purposes. This "B" bile, most

* Read at the Fifth International Congress of Radiology, Chicago, Ill., Sept. 13–17, 1937.
† Deceased.

TABLE I. GROUP A

COMPARISON OF CHOLECYSTOGRAPHY AND DUODENAL DRAINAGE IN DIAGNOSIS OF GALLSTONES
33 CASES IN WHICH GALLSTONES WERE FOUND AT SURGERY OR AUTOPSY

	Case No.	Primary Film	Cholecystography*	Duodenal Drainage	Surgical Findings
1	1	Stones	Not visible	Pigment and crystals	Numerous stones
2	7	Stones	Faint	Pigment and crystals	Filled with small stones
3	8	Stones	o	Cholesterol crystals	Filled with stones
4	11	Stones	o	Pigment and crystals	Filled with stones
5	12	Stones	Clear	Pigment and crystals	Several stones
6	16	Stones	o	Pigment and crystals	One stone
7	20	Stones	Clear	Pigment	Many stones
8	26	Stones	o	Pigment and crystals	Many stones in gallbladder, one in common duct
9	27	Stones	o	Pigment and crystals	Many stones
10	32	Stones	o	Pigment and crystals	Few stones
11	33	Stones	o	Pigment and crystals	Many stones, one in common duct
12	5	Stones	Faint	Negative	Two small stones
13	6	o	Clear and stones	Pigment and crystals	Many small stones
14	17	o	Faint and stones ?	Pigment and crystals	Few stones
15	29	o	Faint and stones ?	Pigment and crystals	Two stones
16	9	o	Clear and stones	Negative	Many stones
17	18	o	Faint and stones ?	Pigment and crystals	Many stones
18	22	o	Clear and stones	Pigment and crystals	Many stones
19	2	o	Not visible	Pigment and crystals	Ten stones
20	3	o	Faint	Pigment and crystals	Many stones
21	4	o	Clear	Pigment	One large stone
22	10	o	Faint	Pigment and crystals	Many stones
23	13	o	Faint	Pigment and crystals	Many stones
24	14	o	Not visible	Pigment and crystals	One stone
25	15	o	Clear	Negative	Few small stones
26	19	o	Faint	Pigment and crystals	Many stones
27	21	o	Not visible	Pigment and crystals	Stones
28	23	o	Faint	Pigment and crystals	Many stones
29	24	o	Faint	Pigment and crystals	Many stones
30	25	o	Faint	Negative	Many small stones
31	28	o	Not visible	Pigment and crystals	Many stones
32	31	o	Clear	Negative	Many stones
33	30	o	Clear	Pigment	Many small stones

* Gallstones were demonstrated on the preliminary films in 7 cases in which cholecystography was omitted (Nos. 8, 11, 16, 26, 27, 32 and 33).

authorities agree, comes from the gallbladder. In this series the bile obtained from the duodenum was examined microscopically after being centrifuged, first, for pigment and crystals which are indicative of the presence of stones in the gallbladder and biliary ducts, and second, for the amount of "B" bile present. When "B" bile was obtained in amounts ranging from 30 to 50 cc. the gallbladder function was considered normal and conclusions were drawn as to the presence or absence of stones in the gallbladder. When "B" bile is absent, or only a slight trace is recovered after repeated drainages, it may be impossible to draw any conclusions about the presence or absence of stones in the gallbladder. Occasionally pigment and crystals may be found in the absence of "B" bile. This is considered indicative of intraductal stones or biliary stasis.

The calcium bilirubinate pigment is seen as an amorphous, lustrous, golden yellow, or orange colored substance, occurring in groups or granules. Cholesterol crystals are colorless, flat and rectangular. They occur in various sizes and often are found in large groups or masses. The find-

TABLE II. GROUP B

COMPARISON OF FUNCTION BY CHOLECYSTOGRAPHY AND DUODENAL DRAINAGE
21 CASES IN WHICH GALLSTONES WERE NOT FOUND AT SURGERY OR AUTOPSY

	Case No.	Cholecystography	Fat Response	Duodenal Drainage			Surgical and Pathological Findings
				No. of Times	Amount of "B" Bile	Pigment and Crystals	
1	2	Clear visible	Good	6	45 cc.	Pigment and crystals	Pericholecystitis with marked fibrosis of gallbladder wall
2	3	Faint visible	—	1	30 cc.	0	Gallbladder densely adherent to duodenum and stomach. Wall not remarkable
3	7	Not visible	—	1	30 cc.	Pigment and crystals	Gallbladder adhesions to hepatic flexure; wall not remarkable
4	8	Clear	Good	1	30 cc.	0	Thin walled gallbladder. Pathologically not remarkable
5	10	Clear	Delayed	1	30 cc.	0	Gallbladder opened and explored. Biopsy of wall not remarkable
6	13	Clear	Good	10	30 cc.	Pigment and crystals	Gallbladder adhesions to omentum. Pathologically not remarkable
7	15	Faint	None	1	Trace	0	Gallbladder thin walled. Pathologically not remarkable
8	18	Clear	Good	2	30 cc.	Pigment and crystals	Thin walled. Emptied easily, not opened
9	21	Not visible	—	1	30 cc.	0	Thin walled. Pathologically not remarkable
10	1	Faint	—	3	30 cc.	Pigment and crystals	Thin walled. Pathologically not remarkable
11	4	Clear	Good	1	15 cc.	Crystals	Thin walled. Pathologically not remarkable
12	5	Clear	Good	1	30 cc.	0	Thin walled. Emptied easily. Not removed
13	6	Clear	Good	4	45 cc.	0	Thin walled. Pathologically not remarkable
14	9	Not	—	3	45 cc.	0	Thin walled. Pathologically not remarkable (cancer, stomach)
15	11	Clear	Good	1	30 cc.	0	Thin walled. Emptied easily. Not removed. (Cancer hepatic flexure)
16	14	Clear	Good	3	30 cc.	0	Thin walled. Emptied easily. Not removed (Cancer pancreas)
17	16	Not visible	—	2	15 cc.	0	Pathologically not remarkable. (Pancreatic cyst)
18	19	Not visible	—	1	0	Pigment	Not remarkable. Mitral stenosis. (Chronic passive congestion of liver)
19	20	Faint	—	1	30 cc.	0	Not remarkable. Primary cancer of liver
20	12	Clear	Good	2	30 cc.	0	Thin walled. Pathologically not remarkable
21	17	Clear	Good	2	30 cc.	0	Thin walled. Pathologically not remarkable

ing of cholesterol crystals or calcium bilirubinate pigment, or both, in the same sediment was considered as evidence of the presence of calculi in the biliary tract.

The fifty-four cases were divided into two groups.

A: Those in which gallstones were found at surgery or autopsy, 33 in number.

B: Those in which gallstones were not found at surgery or autopsy, 21 in number.

Group A. In 33 cases in which gallstones were found at surgery or autopsy a positive diagnosis was made roentgenographically by actual demonstration of the stone

shadows, 15 times. Suggestive, but not positive, evidence was observed in 3 additional cases. In this group the primary films made the positive diagnosis of cholelithiasis in the majority of cases, and cholecystography helped to establish definite evidence of stone shadows in only 3 cases, when they were absent on the primary films.

The diagnosis of calculi by means of duodenal drainage was positive in 28 of the 33 cases. This figure approximates the reports of other workers. The positive identification of stone shadows, when they are present, was accomplished by roentgen examination in 45.5 per cent of the cases, while duodenal drainage gave evidence of stones in the biliary tract in 85 per cent of the cases.

On further analysis it was noted that the tests coincided in their findings in 16 cases. In the remaining 17, however, they were at variance. Both tests made a positive diagnosis of gallstones in 13 instances, roentgen ray in 2, when duodenal drainage failed to reveal their presence. Drainage showed gallstones 15 times when the roentgen ray failed to demonstrate their shadows. Both methods gave no positive evidence of calculi in 3 of the 33 cases. Both tests have limitations in their ability to diagnose the presence of stones. Cholecystography produced good visualization without demonstrating stone shadows in 4 instances in which stones were present while, on the other hand, duodenal drainage produced normal amounts of "B" bile and no pigment and crystals after repeated drainages in 4 other cases. when stones were present.

Group B. In no instance did cholecystography reveal stone shadows while duodenal drainage made a diagnosis of gallstones in 7 cases when they were not present. The fact that the presence of pigment and crystals can be found in individuals without gallstones has been previously reported by Bockus and his coworkers.[4] Duodenal drainage revealed evidence of gallstones in 7 cases. Five times pigment and crystals were found in the duodenal contents for no accountable reason after surgical exploration of the biliary tract and microscopic study of the gallbladder wall.

In one instance the precipitation of pigment could have been accounted for by the fact that the individual was deeply jaundiced, due to chronic passive congestion of the liver, and in another the pigment could have been accounted for by severe cholecystic disease without stones.

SUMMARY

1. In the presence of gallstones roentgenography made a positive diagnosis only 15 times, 12 on the primary films and 3 on the cholecystograms, while duodenal drainage made a positive diagnosis 28 times in a group of 33 surgically proved cases.

2. In the 21 cases in which no gallstones were found at surgery the roentgen examination did not reveal shadows of calculi in a single instance. Duodenal drainage indicated the presence of calculi in the biliary tract 6 times in the 21 cases when no stones were present at surgery.

3. Roentgen examination failed to detect the presence of calculi at times when they were present. Of paramount significance, however, is the fact that roentgen examination was negative in the entire group in which no stones were found at surgery.

4. A positive diagnosis of stones was made by duodenal drainage at times when no stones were present.

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Vol. 44, No. 2

ECHINOCOCCUS CYST OF THE LEFT LOBE OF THE LIVER

REPORT OF A CASE

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ECHINOCOCCUS disease is of infrequent occurrence in the United States. Its limitation to the left lobe of the liver is unusual. This communication reports such a case in which the diagnosis was made in the course of a roentgenological examination.

The patient, a Jewish male dentist, aged forty-five, was born in Poland but had been living in Chicago for the past thirty years. When first seen on January 25, 1937, he had been complaining for some three weeks of a gnawing pain in the right upper quadrant which radiated to the back and up towards the right shoulder. The pain was not accompanied by nausea, vomiting, chills, fever, or jaundice and had no relation to the intake of food. At times epigastric discomfort of a moderate degree either occurred independently or was associated with the above pain. Numerous bowel movements without diarrhea might accompany or frequently precede these attacks. Belching was a prominent symptom.

Further questioning elicited a history of similar symptoms over a period of twenty-five to thirty years. Twenty-five years ago a diagnosis of a peptic ulcer was made. Eight years ago a roentgenoscopic examination by a prominent internist revealed no evidence of a peptic ulcer, and no mention of any cyst was made. In April, 1936, a similar attack occurred. Other than the above the past history is of no consequence.

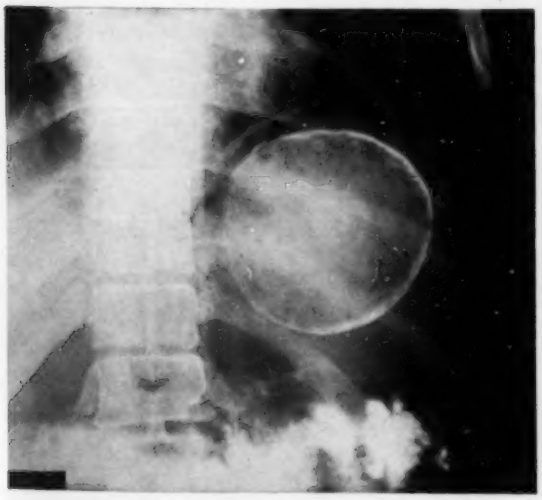

FIG. 1. Anteroposterior view. Calcified cysts and daughter cysts.

FIG. 2. Posteroanterior view. Shows relation of cyst to stomach.

Physical examination in January, 1937, revealed a rather obese patient weighing 186 pounds. The blood pressure was 130/90. Urinalysis revealed normal findings. No abnormal physical signs were elicited. The impression was gallbladder disease although the history and findings were not typical. On roentgenological examination the gallbladder (double dose method followed by a repeat single dose) was not visualized.

In May, 1937, the patient again complained of intermittent epigastric distress, only partly and temporarily relieved by alkalies. The weight was 181 pounds and the blood pressure 134/90. The physical examination was again essentially negative.

In view of the past history and the recur-

Fig. 3. Lateral view. Shows degree of compression of stomach by cyst.

rence of symptoms and in spite of the fact that a diseased gallbladder had been demonstrated, a roentgen examination of the stomach was deemed advisable. This examination revealed no evidence of any intrinsic abnormality of the stomach or duodenum. However, a round shadow, about 9 cm. in diameter, and several smaller densities were discovered. These shadows, which had the density of calcium deposits, were definitely free of any connection with the left kidney or the spleen. The large one lay posterior to and slightly compressed the stomach. These densities were interpreted as being calcified echinococcus cysts in the left lobe of the liver.

The complement fixation test for echinococcus disease was negative and no material for the intradermal test was available. Examination of the blood revealed 95 per cent hemoglobin (Dare), red blood cells 5,200,000, white blood cells 10,400, and a differential count of 72 per cent neutrophiles, 27 per cent lymphocytes, and only 1 per cent eosinophiles.

Analysis of the above data led to the conclusion that these symptoms were due to disease of the gallbladder and that the presence of the cysts was merely an incidental finding. It is noteworthy that echinococcus disease may never produce clinical symptoms.

SUMMARY

A case is reported of an apparently asymptomatic calcified echinococcus cyst with several calcified daughter cysts in the left lobe of the liver. The diagnosis was made incidentally in the course of a roentgenological examination.

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Vol. 44, No. 2

ON THE NATURE OF CALCIFIED LESIONS

WITH SPECIAL REFERENCE TO THOSE IN THE SPLEEN*

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CALCIFIED lesions within the body are frequently observed on roentgenological examination, particularly those within the thorax, in the regions of the liver and kidneys, and to a less extent in the regions of the mesenteric lymph nodes, spleen and pelvis. Outside of calcareous deposits in secretory and excretory ducts, most of these calcifications are usually thought to be tuberculous in origin. Nevertheless, it is not always easy to distinguish them during life. Many large calcified tuberculous mesenteric lymph nodes may be confused with kidney or gall stones. Small discrete calcified lesions are frequently observed on each side of the pelvis that are predominantly phleboliths in the veins, around the genitourinary organs, but they may be confused with calcified tubercles. Similar appearing lesions exist in the region of the spleen and within the spleen, about which opinion is divided regarding their nature.

In an attempt to clear up the status of these lesions, a study of calcifications in general and those of the spleen in particular has been made on a selected series of cases coming to autopsy, and will be reported in the following pages.

As the literature on pathological calcifications is extensive, a complete review of the subject will not be attempted here. For this the reader will be referred to the relatively recent bibliographies by Barr,[1] Puder,[17] Wells,[23] Schmidt,[19] Kleinmann[9] and Spitz.[20]

The important feature is that the causes of most calcifications may be identified pathologically without difficulty. It is rare that any of these foreign calcifications simulate the course of a primary tuberculous complex and, in this country at least, are not nearly as frequent. Calcified cysts have a capsule around an irregular calcification, both of which are different from a tuberculous lesion. In the central mass are almost always found elements that are pathognomonic of the particular condition, hair, teeth, echinococcus hooklets, gallstones, etc. Cysts in the pancreas are irregular in shape and density, have a homogeneous calcified central mass that shells out *in toto*, with no resorption, and a heavy fibrous wall usually with the remnants of a duct wall within. They have no resemblance to and little in common with tubercles. Calcified hemorrhages are usually massive, irregular in shape, and entirely unlike a tuberculous calcification. Kidney stones nearly always conform to the shape of the pelvis or ureters, and shell out like a kernel from a nut.

Of the non-tuberculous calcified lesions, however, not all are so easily differentiated, because among others, phleboliths may consistently resemble tubercles in shape and size. They are common around the genitourinary apparatus and occasionally around the spleen. The roentgenogram usually shows them just inside the pelvis at the right side of the genitourinary apparatus as almost perfect spherical soft shadows. In fact the more perfectly spheroid, the more thay are apt to be phleboliths. Microscopically the walls of the vessel are distinct and the central mass is usually different from tubercles.

Of the various locations of calcified lesions in the body none is more controversial than the small, single or multiple calcifications of the spleen. Inasmuch as the spleen is the crossroads of so many diseases, a thorough investigation of such lesions is

* Read in part before the Chicago Tuberculosis Society, May 11, 1939.

considered timely to determine the major cause. It also affords an excellent opportunity to follow the morphological changes with increasing age, and test the age-morphology theory which I have advanced before.[21]

The spleen is affected more with tuberculous calcification and perhaps less with non-tuberculous calcification than any other abdominal organ. About 20 per cent of the spleens of our postmortem series on tuberculous patients show calcifications. According to these studies, about 1 in every 5 patients has one or more, and about one-half of these (1 in 10) have multiple calcifications ranging from a few to hundreds. A part of these findings were reported with Martinsen.[22]

Although there were many reports before, one of the best early reports was in 1912, when Winternitz[24] reviewed the subject of "primary" tuberculosis of the spleen. By adding 11 cases to the reports of others, he was able to compile a series of 51 cases where the first and only clinical manifestation of the disease was in the spleen. The symptoms were pain in the splenic region, fever, large spleen, and usually severe symptoms until the organ was removed. The significance here is that these acute forms in the spleen may represent the antecedent condition for calcifications which may exist even without signs of disease elsewhere, or without any clinical disease at all. One similar case was reported by Moorman[11] in 1937 where the spleen was removed about twenty-two years after the symptoms, and the lesions corresponded to what appeared to be an ancient hematogenous tuberculosis.

The opinions expressed in the literature concerning such calcifications in the spleen, however, are about evenly divided between phleboliths and tubercles. In favor of phleboliths, Polgár and Szemzö[15] in 1926 reported a case where the roentgenogram showed about 100 discrete calcified nodules in the spleen with a smaller number in the liver. Although their argument was far from convincing they considered that the lesions were phleboliths. Koppenstein[10] in 1928 reported 8 cases in adults which were thought to be phleboliths. The past histories of 7 were as follows: 4 had typhus, 1 syphilis, 1 eclampsia, and 1 dysentery. The youngest was thirty-two years old. Bársony and Schütz[2] in 1931 routinely roentgenographed 180 spleens from autopsies and found 7 with multiple calcifications which they called phleboliths, after a histological examination. All were in old persons. In 7 tuberculous cases there were no calcifications, which is of little significance. It is granted that some or all of these cases may be phleboliths, but the evidence produced is by no means absolute. Berman[3] in 1937 reported 10 cases, 7 of which were in old people. He also felt that the majority were phleboliths.

For the rarer causes of calcification of the spleen the reports of Mount, Mount and Hunter[12] on a calcified massive hemorrhage; Földes[6] for calcified cysts; Holl[7] for calcified echinococcus; Pick[14] for bone tumors; and Ponzio[16] for calcified hemangiomas and lymphangiomas, reveal that none of these conditions should cause any difficulty in a differential diagnosis of small multiple calcifications. Nor should calcified infarcts and abscesses cause any difficulty if a good history is taken.

In favor of a tuberculous nature, Courtin and Duken[5] in 1928 reported 3 cases of spleen calcifications in children that were considered to be tuberculous. The lesions corresponded to the stage of hematogenous dissemination of the primary infection. Hrbek[8] and Ruhnau[18] reported similar cases. Spitz[20] even reported a case in an adult where the calcified foci apparently corresponded to the stage of hematogenous spread from a primary lesion in the lung. He also pointed out the difficulties in making a roentgenological diagnosis without a stereoroentgenogram. Bunch[4] also described multiple calcifications in the spleen of a woman, aged thirty-eight. The organ resembled Banti's disease, but on section

it proved to be tuberculosis. Then there is the case reported by Moorman[11] referred to before. As previously mentioned also, Sweany and Martinsen[22] reported 26 of 132 cases with calcifications in the spleen, most of which were thought to be tuberculous. In a recent survey of a larger number in tuberculous patients, 19 per cent were found to have spleen calcifications. Von Orelli[13] recently made a report of 4 cases where 3 were found to be tuberculous by microscopic section, and the other, although not sectioned, was thought to be similar.

In my studies in a large series of cases the evidence has been practically all in favor of tuberculosis as the cause of spleen calcifications. First, they are within the spleen parenchyma and not in the splenic veins outside the spleen, or in the trabeculae where phleboliths are wont to appear. Most of them are multiple and seem to be from hematogenous dissemination. Many of each group are two to three times the size of the largest veins and therefore too large to be phleboliths. They are *all* associated with and correspond roughly in age characteristics to a primary complex elsewhere (either in the neck, lung, or mesentery). Therefore, they would probably correspond to the hematogenous phase of the primary infection. They are in tuberculous individuals, most of whom show a continuous progression of tuberculous disease, and the great majority are also free from pathological and serological evidence of syphilis or concrete evidence of other interfering diseases. They have no microscopical resemblance to phleboliths where the vascular walls of smooth muscle may be seen and the internal structure is different from tubercles.

In order to verify these facts, however, a selected series of cases has been carefully studied with the purpose of showing a transition from early tubercles to all ages of the old calcified types. All possible ages of lesions are included, most of which are in the spleen, but a few liver tubercles are included in passing.

The character of the early lesion is not unlike those described for early tubercles elsewhere in a separate report.[21] Only 2 early cases will be included to show the characteristic capsule development.

Case I was an eight month old lesion in an eleven month old infant. It was given as Case 6 in Chapter I in a former report.[21]

Case II is a fifteen month old lesion, shown in Chapter I, Plate II (Figs. 1 and 2) of the same report. Younger lesions have correspondingly less capsule and more of the inflammatory elements. Some of these early lesions are shown in Case III of the present study along with the older lesions.

In this study I am obliged to emphasize principally lesions after they have begun to calcify and proceed to those of twenty or more years old. The early lesions are more definite because they are specific in morphology and contain tubercle bacilli. The important feature is that they are identical in every way to older tubercles except in the specific elements.

Case III. A. R. (A409) was a colored boy, aged nine, whose sister had tuberculosis of the hip. There was no other known tuberculosis in the family (Fig. 1).

His onset was as a "cold" one and a half years before death. The cough persisted, he lost weight, became listless. A diagnosis was made nine months before death. In addition to the terminal findings there was: In the right lower lobe a small partially calcified parenchymal lesion measuring about 3 mm. and an extensive enlargement of the lymph nodes of the bronchi and the right side of the trachea, which contained much calcium. On the left side of the trachea above the bifurcation was a much enlarged group of calcified nodes. They seemed to be the largest group and the oldest lesions present. Practically all the other nodes were fibrocaseous with a slight ring of calcification usually found in two year lesions. The secondary lesions were disseminated throughout the lungs and consisted of miliary to nodular tubercles, characteristic of a hematogenous spread of infection (Fig. 2).

There were about 150-200 lesions 1.5 to 3 mm. in size in the spleen and also many in the

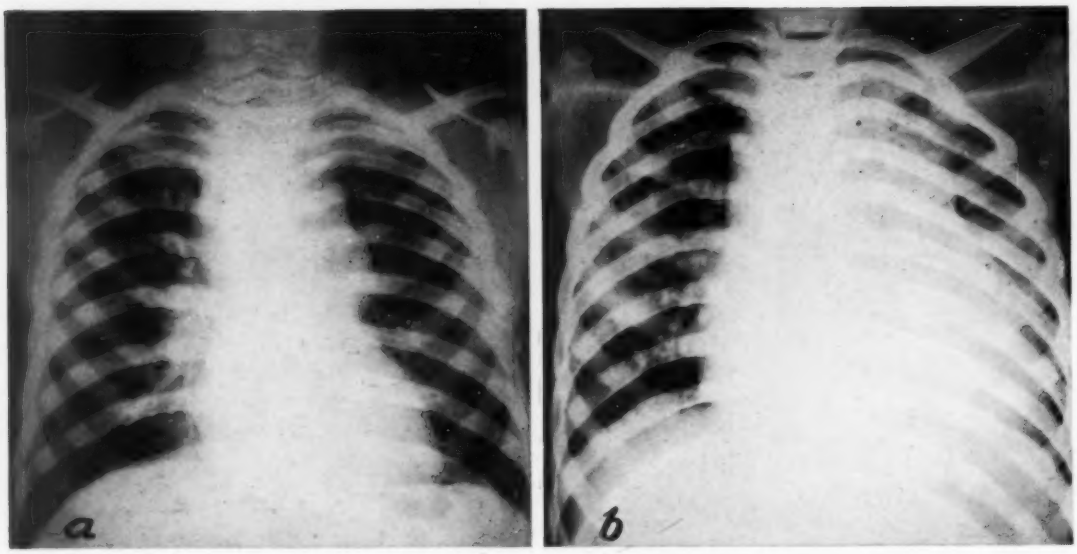

Fig. 1. *a*, roentgenogram of Case III taken on February 27, 1930. Note hilar lymph node enlargement. *b*, same as *a*, taken July 12, 1930, showing marked extension of process in the hilum and also into the parenchyma.

liver. The roentgenogram revealed only six to eight in the spleen that were calcified. These lesions were irregular in outline. The ages of the calcified lesions in the lungs and the spleen are the same general age type—two to three years. In the spleen, however, there were many having more recent age types of one and a half and one year, and even recent tubercles, indicating that

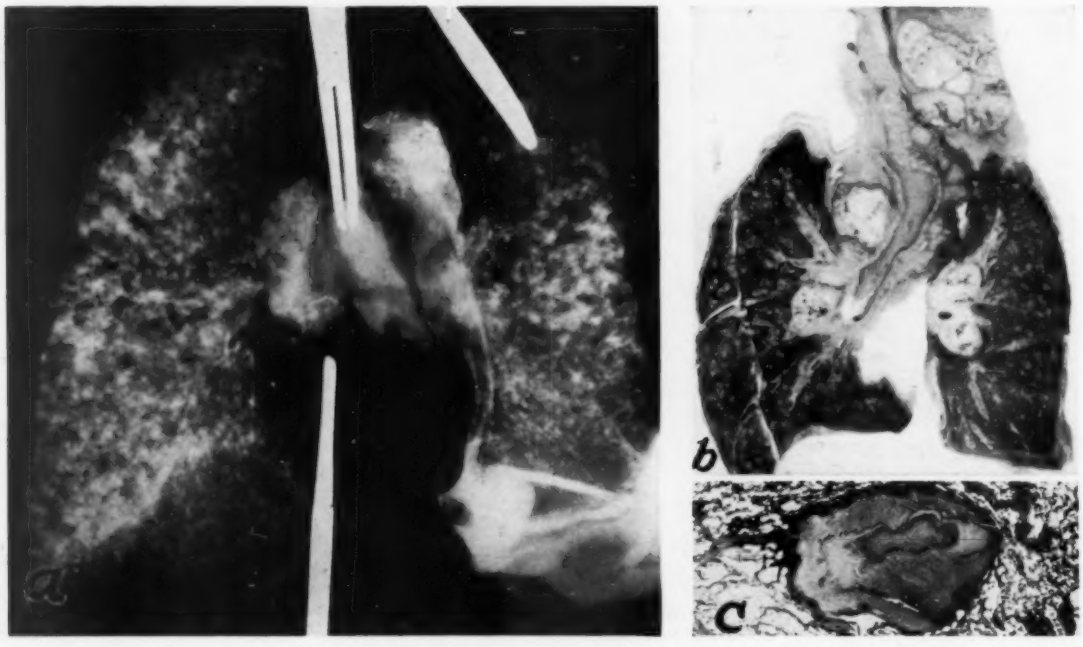

Fig. 2. *a*, postmortem roentgenogram of lung and hilar lymph nodes. *b*, gross photograph of a sagittal section. *c*, photomicrograph of local parenchymal lesion. A two to three year type. (×8.5, hematoxylin and eosin.)

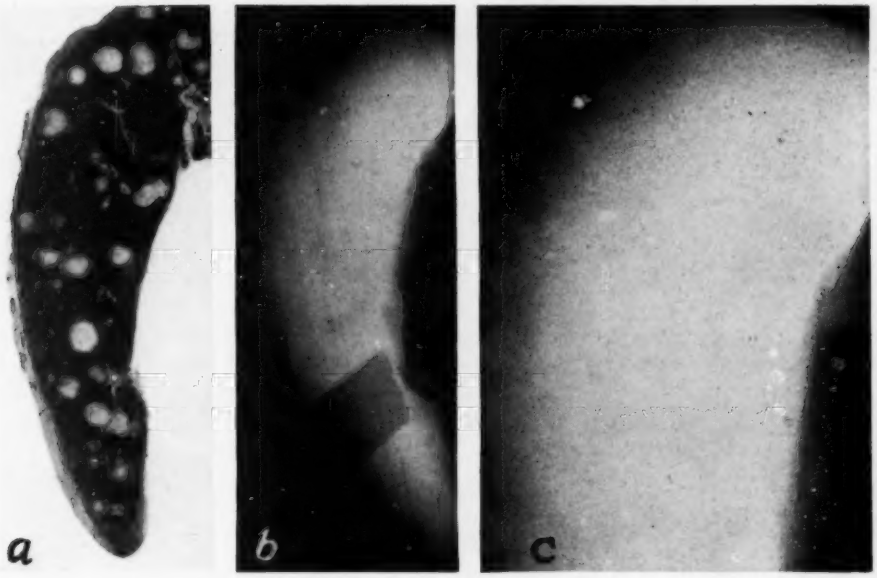

Fig. 3. *a*, gross photograph of a sagittal section of the spleen. *b*, postmortem roentgenogram of same section of spleen. *c*, same as *b* with enlarged upper end, showing a few calcifications. ×2.2.

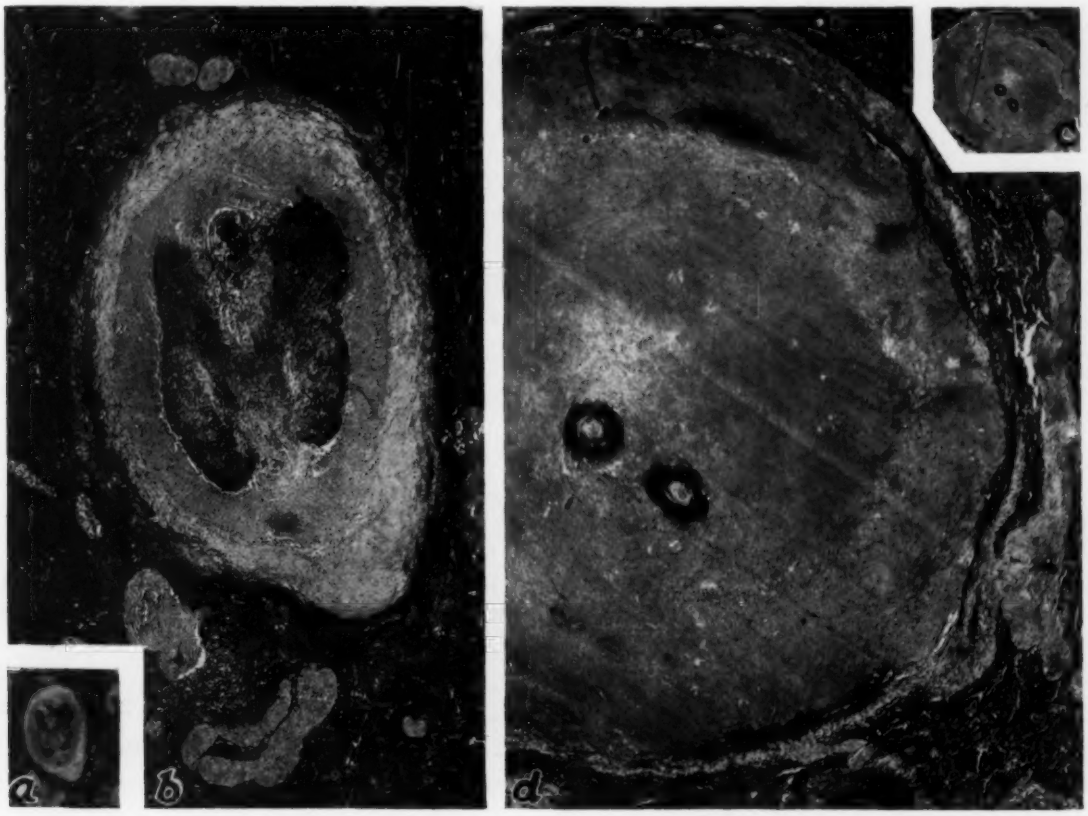

Fig. 4. *a*, photomicrograph of a spleen tubercle with calcified center. ×8.5. *b*, same as *a*. ×45. Note perceptible fibrous capsule; not over three years old. *c*, a more recent tubercle. ×8.5. *d*, same as *c*. ×45. Very little capsule. A two to three year type. (All hematoxylin and eosin.)

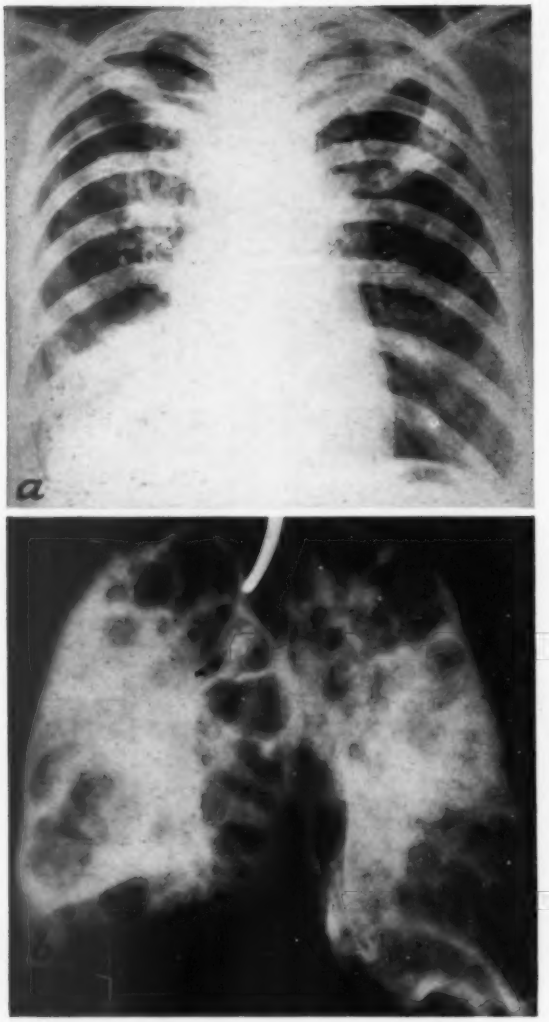

Fig. 5. *a*, antemortem roentgenogram of Case IV taken July 21, 1938. *b*, postmortem roentgenogram showing one large calcified lesion. Taken March 7, 1939.

the dissemination in the spleen extended over many months as in the lungs and adjacent lymph nodes (Fig. 3).

Comment. The fact that the child was colored may account for the longer period of generalization. The evidence of tuberculosis in all these lesions is absolute (Fig. 4).

Case IV. L. C. (A1197) was an American girl, aged twenty-four, with uneventful early history. She worked in a cigar factory one year, then was married at nineteen, after which she worked as a waitress four years. In the fall of 1937 there was a long succession of events. She worried a great deal about marital affairs, left her husband, roomed with a sister (who later developed tuberculosis), had a right-sided pleurisy (in November, 1937, gonorrhea (in December, 1937), and her (second) doctor made a diagnosis of tuberculosis in March, 1938. She died one year later as the result of a slowly progressive primary tuberculosis about seven years after leaving home to go to work (Figs. 5 and 6).

The lung and lymph node tubercles are the five year type and are almost identical with the oldest calcified lesions of the spleen from which cultures of tubercle bacilli were obtained. The lesions, about 200 in number, are very slightly older than in Case 1. The spleen tubercles were

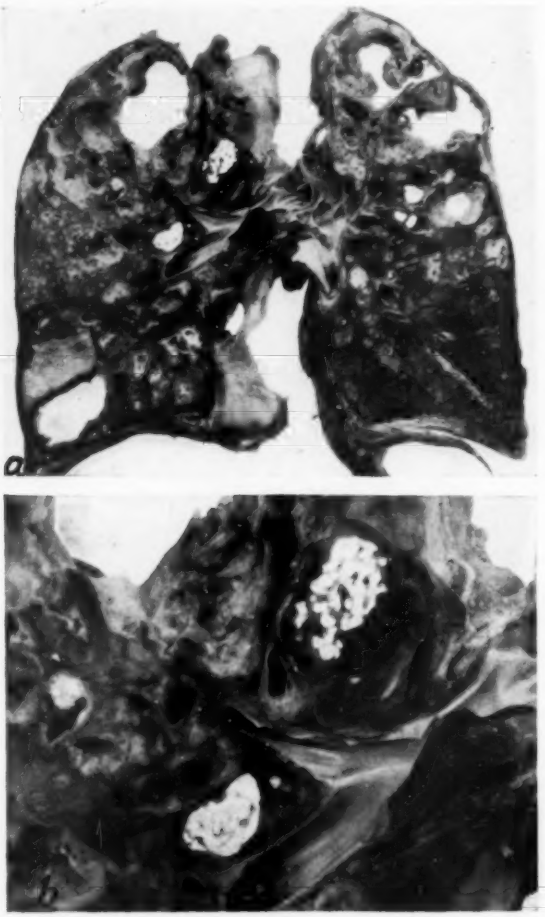

Fig. 6. *a*, photograph of sagittal gross section of Case IV. Note soft calcified primary lesions. *b*, enlarged section at the hilum showing three soft calcifications. The parenchymal lesion shows an opening into a bronchus.

obviously not all of the same age. Some were the five to six year type, having calcified centers. Only seven of these tubercles showed calcium on the postmortem roentgenogram, the shadows of which were irregular in outline. Other tubercles were of the three to four year type. It seems, therefore, that the dissemination to the spleen was spread over several years' time, while the primary process was progressing to maturity. Instead of healing there was a definite parenchymal spread in the lung that led to her disease and death. The evidence of tuberculosis in the splenic lesions is absolute (Figs. 7 and 8).

Case v. M. W. (A1038) was an American female, aged thirty at the time of her death. She came to Chicago from Indiana at the age of twenty, and was married. She had an appendectomy in 1929, a cesarean section in 1931, and removal of the tubes in 1934. The onset of tuberculosis was in 1936 and she died in 1937.

There were many small soft calcifications around a large cavity in the right upper lung lobe and a large 1 cm. calcification in the hilum "about five years old." There was also one nearly round calcified lesion in the spleen about 5 mm. in diameter. The age of the spleen tubercle was of a twelve year type. It suggests one of the following possibilities: The oldest lymph node lesion was not found; there was an earlier hematogenous spread of tuberculosis; there was a small hemorrhage that calcified; or it was a phlebolith.

Comment. In spite of all the other possibilities, the most probable cause of such a calcified lesion in the spleen is tuberculosis. The morphology, size and microscopical character is typical. The age character of the lung lesion, however, did not correspond to the age character of the lesions in the spleen.

Case vi. J. M. (A1093) was an American female aged twenty-seven at death. A sister had a productive cough for four years before the death of this patient, but the diagnosis in the sister was not made until after this patient's disease was found two years before death. The sister is still living. The infection would perhaps have been about six years before if she obtained it from her sister. However, both may have obtained their infections from a common source near that time.

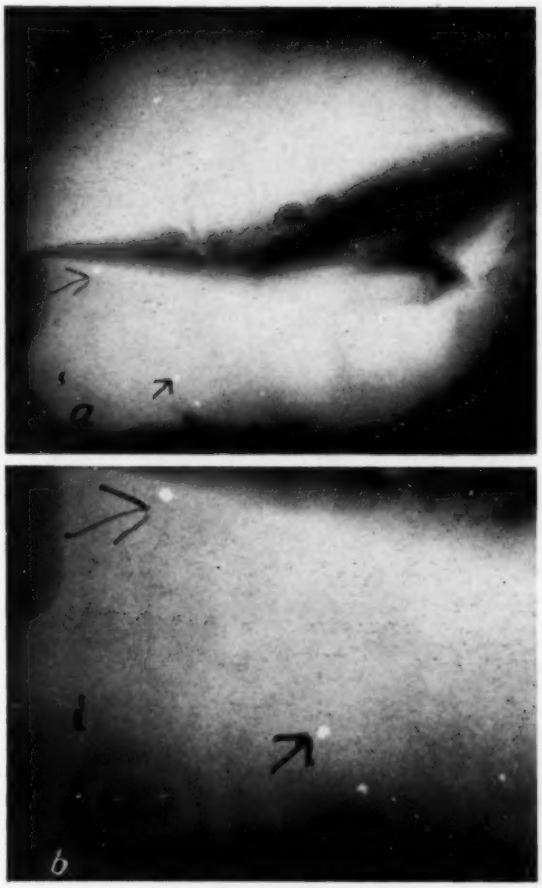

Fig. 7. *a*, postmortem roentgenogram of spleen of Case iv. *b*, enlarged segment showing calcification. ×2.2.

In the right lung there were small 2 mm. parenchymal calcifications and several large hilar calcifications. There were many thin-walled cavities throughout both upper lobes and the upper portions of the lower lobes. Between these were many acinous-nodose, bronchopneumonic and fibroid lesions. There was a lung stone in the bronchus leading to the large cavity in the right upper. The lymph nodes were somewhat hyperplastic and anthracotic. There were ulcers in the trachea and bronchi almost up to the larynx. The spleen contained seventeen rather irregular calcifications from 2-4 mm. in diameter.

Comment. The calcified lesions were of the five to six year type, including those in the spleen. All the evidence is in favor of its being tuberculosis throughout.

Case vii. A. R. (A1163) was an American

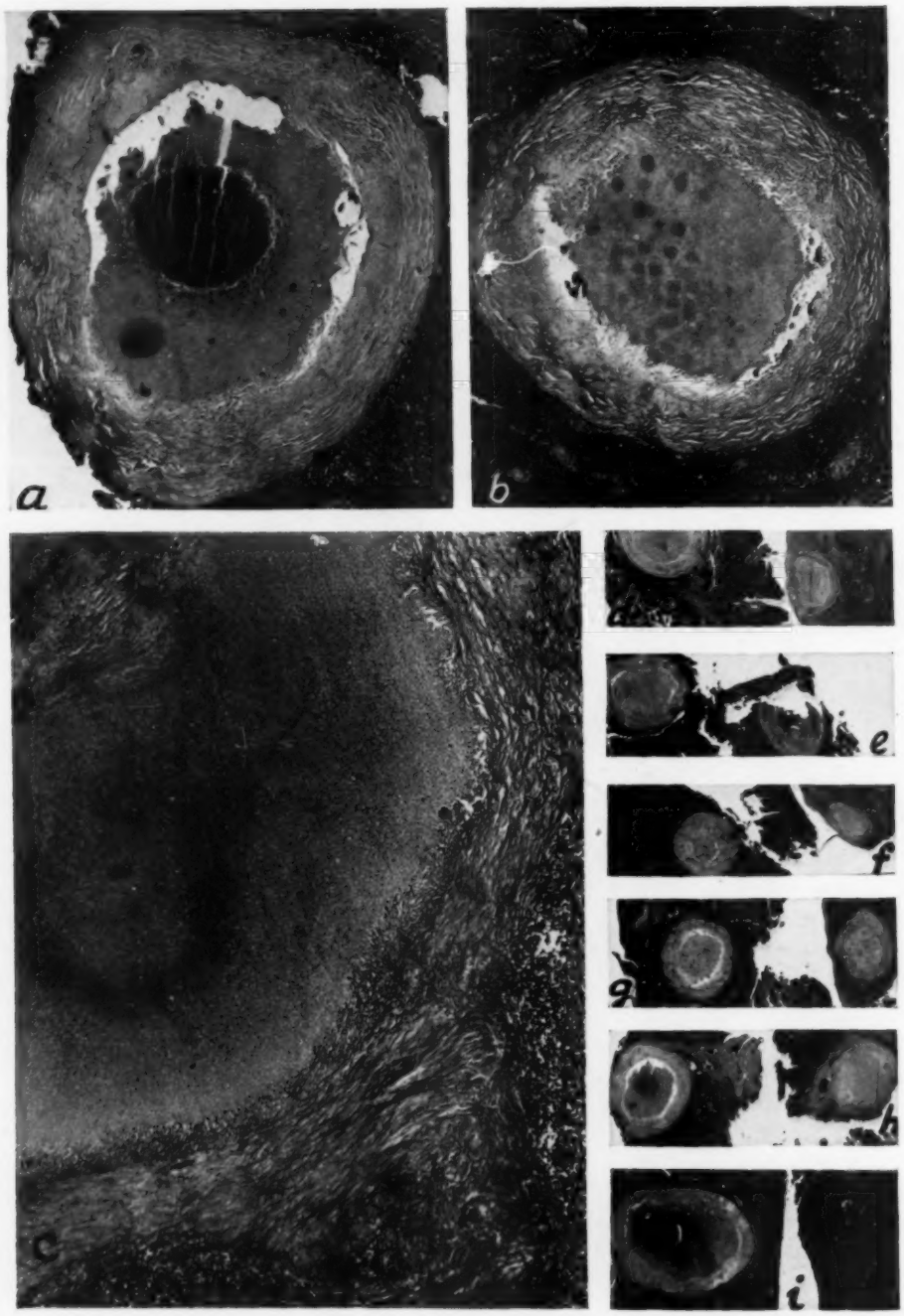

Fig. 8. *a*, photomicrograph of spleen tubercle with a calcified center. ×45. *b*, same without a calcified center. ×45. Note moderately heavy capsule. *c*, a tubercle from the bronchopulmonary lymph nodes. ×45. Note similarity to spleen tubercles. *d*, *e*, *f*, *g*, *h*, *i*, various spleen tubercles. ×8.5. (All hematoxylin and eosin.) A five to six year type.

male, aged twenty-six at the time of death. There was no history of contact except with a tuberculous girl beginning seven years before his death.

The significant pathological findings reveal the following: There were a few small primary calcifications in the left upper lobe and a definite fibroid cavity in the center. This cavity

may be the location of the first infection. There was a definite calcified lymph node involving the nodes in the superior mediastinum, in direct relationship to the cavities, and calcifications in the left upper lobe, but nothing at the hilum. There was a more recent spread in the left base and in the right upper and middle lung lobes. The right upper lobe was made up of a fibroid cavity filling most of the lobe, and a cavity in the middle lobe that formed a bronchopleural fistula, a pyogenic membrane covered the whole lung. There was apparently a hematogenous spread to the spleen consisting of fifteen irregular calcifications of 2-4 mm. in diameter. The ages of the calcified lesions, including those in the spleen, are about six years.

Comment. The evidence is all in favor of tuberculosis.

Case viii. I. W. (A1166) was a colored male, aged nineteen at the time of death. The only complaint was a pain in the right shoulder two years before death. A diagnosis was made at the Cook County Hospital in May, 1938, of a tuberculous infection involving the shoulder clavicle and testicle. He was admitted to the Municipal Tuberculosis Sanitarium in July, 1938, and died in November of the same year.

The pertinent pathology was a rapidly spreading tuberculosis from a tuberculosis in the bronchopulmonary lymph nodes. The point of entrance of the infection must have been in the pulmonary parenchyma out from the outermost lymph node, but there was no evidence found in the tissues. This lymph node was softened and had ulcerated into the right main bronchus. At the point of opening was a 7 mm. ulcer. Above this was a large 10×12 mm. ulcer, 5 mm. deep. It had a clean wall, perhaps the remnant of a completely sloughed out lymph node. The large hilar lymph node was 3×5 cm. and was dry and caseous. A right paratracheal node measured 4×6 cm. There was a gradual decrease in age as the growth extended upward, as indicated by a lack of pigment. In relation to the first large bronchopulmonary fistulous node was a fresh growth protruding anteriorly 7 mm. into the superior vena cava and measuring 10 mm. across at the base. The entire pleura of both sides showed a caseous 0.5 to 1.5 cm. layer of caseous tuberculosis (pleurisy en cuirasse). Both lungs revealed scattered miliary tubercles, about two per high power field. The heart weighed 250 gm. In the wall of the left ventricle on the left border near the apex was a 3 cm. firm, grayish-yellow caseous node. It involved the inner half of the muscle and bulged somewhat into the left ventricle presenting here a smooth, glistening surface. The myocardium was pale brown and softened.

There were recent miliary tubercles in all the organs, four per high power field in the liver, two in the spleen, and one in the kidney. There were two old calcified lesions in the liver of a seven year age character.

The capsule of the oldest lymph node tubercle was indefinite, but suggested a process of three to five years. One and perhaps two of the lymph nodes had excavated leaving a crater. It had been an overflowing process and the true age was not determinable. The isolated calcified nodules in the liver were of the six to seven year type. If they were tuberculous in origin the primary must have occurred in the lungs at about that time, followed by a quick hematogenous spread to the liver and leaving a smoldering process in the bronchopulmonary nodes which gradually spread to the hilum, pleura, heart, vena cava, and then as a terminal general miliary tuberculosis with meningitis.

Comment. This is similar to the type reported with Martinsen[22] where the process in the spleen or liver was called "cryptic" because the point of entrance of the infection was not found. The infection probably went through the lung parenchyma without producing a lesion large enough to find.

It is felt that the lesion in the liver is the result of the first hematogenous spread about six years before death; that the pulmonary parenchymal lesion was too small to leave any trace; that the first main lymph node enlarged slowly over several years, and ruptured destroying the age characteristics.

Case ix. F. T. (A1188) was a colored boy, aged ten at the time of death. He was born in Arkansas and came to Chicago at the age of seven years. There was no known contact with tuberculosis. He had whooping cough at five years and malaria at six years of age. His tuberculosis began in July, 1938, and he died in February, 1939.

The essential postmortem findings were as follows:

In the lungs there were two irregular 7 mm. calcifications in the middle of the left lower lobe near the mid-scapular line with a wide area of perifocal emphysema; several small satellite foci towards the hilum; three 6 mm. calcifications in the bronchopulmonary nodes, and two 1.5 cm. calcified masses in the hilum. The lymph nodes on the right were more recently formed; one contained a large caseous focus with early calcification; others were caseous with heavy capsules, and others with thin capsules. One of these pulmonary lymph nodes about one-third out from the hilum towards the pleura had broken into a bronchus. Two old tubercles were found in the walls of a medium sized vein. There was a fibrous pleuritis encasing the whole right lung. In places there was a thick layer of caseous tuberculous pleuritis and an acinous-nodose and miliary seeding of tubercles throughout the right parenchyma as well as the left. There were no doubt also recent vascular penetrations, but they were not found.

The liver revealed a large number of recent tubercles and one tiny calcification. The spleen contained fifteen irregular calcifications ranging from 1-4 mm. in diameter. These lesions appeared to be in three widely separated age groups. One, of a dense calcified focus with a destruction of the "inner" capsule and part of the "middle" capsule. There was slight resorption and the formation of bosses. The age was estimated as eight to ten years. Another of almost the same density of calcification, but wherein the calcification had not reached the inner capsule, would ordinarily be compared to lung tubercles of six to eight years. The majority of the other tubercles were fibroid miliary tubercles of a more recent age, similar to others seen in cases of about two years' duration. Perhaps there were many "showers" of tubercles extending over a long period of time, but I am inclined to believe that there were only two or three main episodes. One was the primary, another was a growth into the pulmonary vein, another a rupture of the lymph node into the bronchus.

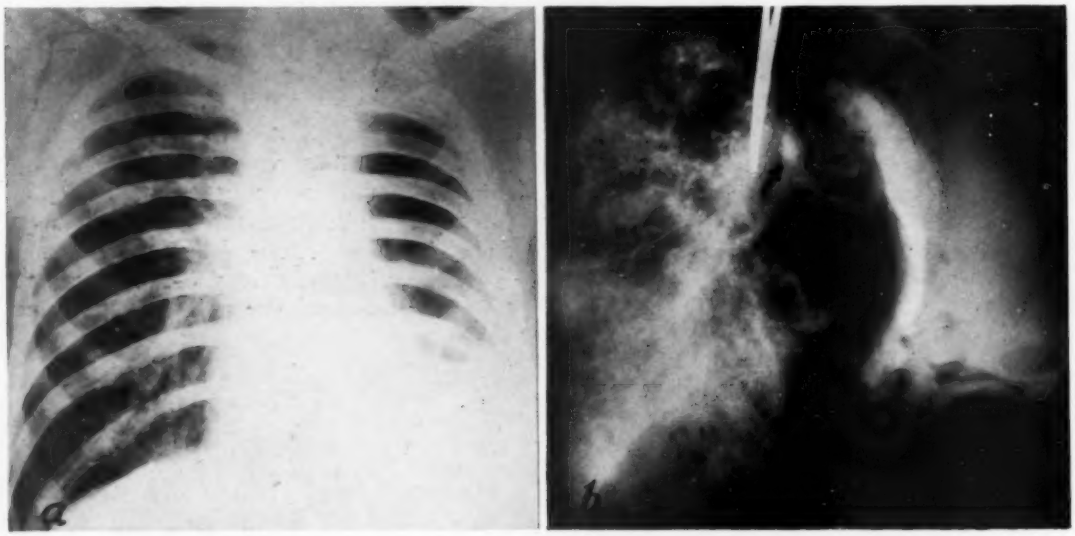

Fig. 9. *a*, antemortem roentgenogram of Case x showing empyema. *b*, postmortem roentgenogram. Note the large calcification at the hilum.

There was also a small duodenal ulcer, a moderate degree of ulcerative tuberculous enteritis around the ileocecal region, a recent tabes mesenterica, several 3 mm. tubercles in the papillae of the kidney, a generalized miliary tuberculosis in all the organs, and a tuberculous leptomeningitis.

Comment. The oldest spleen calcifications are so like those in the lung and lymph nodes that it is no doubt the same tuberculous process. The recent spleen tubercles are no doubt also due to a hematogenous spread from the more recent lesions in the pulmonary veins in the right lung and hilum. There was a slowly progressive process in the lungs as there were tubercles of

age characteristics of approximately ten, eight, five, three, two and one and less than one year.

Case x. H. E. H. (A1140) was an American male, aged thirty-seven at the time of his death. He was in the army six years, a Government clerk 1.5 years, and a cab driver 8.5 years. His wife had asthma for thirteen years, but there was no mention of tuberculosis. The onset of his disease was in 1930. The patient was admitted to the Sanitarium three times and once to the M. T. S. Home. He died in 1938 of pulmonary tuberculosis (Fig. 9).

There was an old cavity in the left upper lobe and a small one in the lingula producing a bronchopleural fistula and empyema on the left side. There were a few small parenchymal calcifications in the right upper, both bases, and a huge calcification in the right paratracheal nodes. *There was a huge mass in the liver with several satellite colonies and twelve irregular, 2-3 mm. tubercles in the spleen*, all of the same age as those in the paratracheal lymph node, and liver (Fig. 10).

Comment. The age types correspond to those of nine to ten year tubercles. All of the lesions are the same general age character and are definitely tuberculous. There is not the character of many episodes which were observed in the last case. It is possible that the wife's "asthma" may have been a tuberculosis (Fig. 11).

Case xi. F. H. (A996) was an American female, aged twenty-three at death. Her father died five years before her own death, of tuberculosis. This case has been reported before as a lymph node type of endogenous spread. The oldest lesion was in the right base and hilum with four ages of lesion in the large paratracheal lymph node. There were many hematogenous lesions in the apexes. The oldest lesions in the lungs and lymph nodes were of the twelve to fifteen year type, and the ten calcified lesions in the spleen corresponded to these in age and size. There was a dense calcified center with a very heavy capsule of great width with water marking of calcification nearly out to the border in several places around the periphery. The ages of the lesions were estimated at twelve to fifteen years (Fig. 12).

Comment. The probability is that her father had the disease for five to ten years before his death and infected the daughter twelve to fifteen years before her death (Figs. 13 and 14).

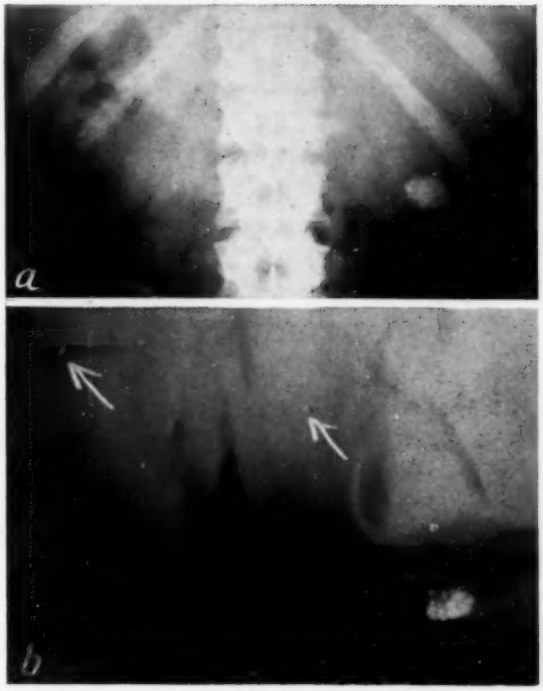

Fig. 10. Case x. *a*, antemortem roentgenogram of upper lumbar region, showing calcified lesions in the region of the spleen, and a huge one in the region of the gallbladder. *b*, postmortem roentgenogram of the liver, showing the large calcified mass in the liver tissue, with two smaller ones.

Case xii. O. A. (A890), male, aged thirty-three at the time of death. He was born in Tucson, Arizona, came to Chicago, married at twenty-five, and was divorced at thirty. He had "malaria at sixteen" and "typhoid fever" the same year. Each disease was reported to be of four months' duration. His tuberculosis began in 1932 and he died in 1936.

In the lungs there were many lung stones in a large cavity in the left upper lobe and a mass of calcifications at the hilum. The oldest lesions were of the fifteen to eighteen year type. There were many calcifications of a less age. The fourteen calcified lesions in the spleen were comparable to those of fifteen years' duration in other cases.

Comment. It is felt that these lesions are all tuberculous in spite of the indefinite history. The question is also raised as to

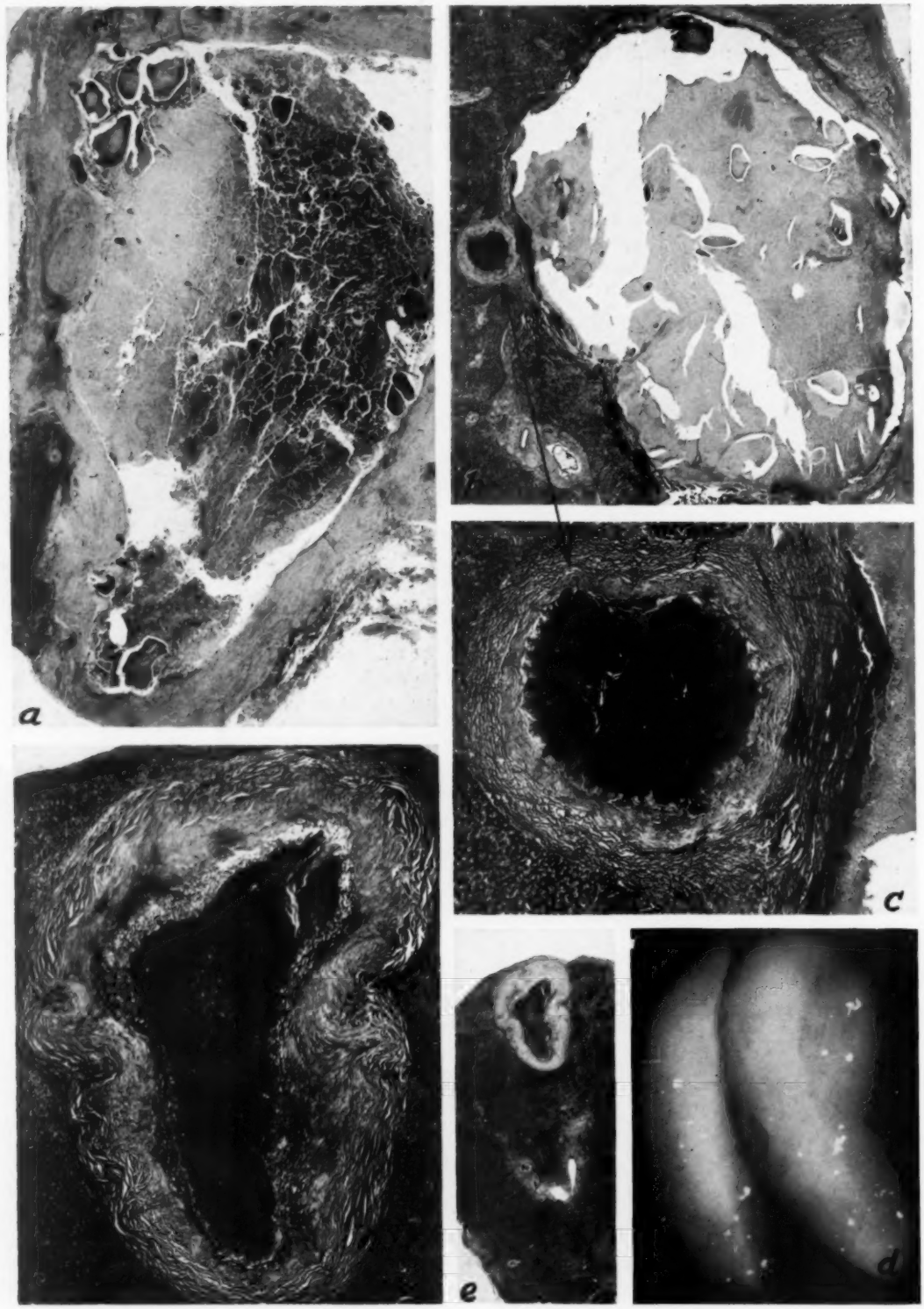

Fig. 11. Case x. *a*, photomicrograph of section of hilar lymph node. Note heavy capsule and islands of dense calcification beginning to form around the border. ×8.5. *b*, photomicrograph of large liver tubercle. Note similarity to bronchial tubercle. ×8.5. *c*, enlarged "daughter" colony of *b*. *d*, postmortem roentgenogram of spleen, showing calcifications. *e*, photomicrograph of calcified tubercle of spleen. ×8.5. *f*, enlargement of *e*. ×45. (Hematoxylin and eosin.) An eight to ten year type.

whether his typhoid and malaria may not have been accompanied by a tuberculosis, or the latter masked as one of them.

Case xiii. M. P. (A507), an American female aged twenty-nine at death. Her mother died of tuberculosis when the patient was ten years old. The infection was, therefore, probably about twenty-one years before her death Her clinical disease lasted sixteen years. There was an apicocaudal spread first from the right apex, then the left apex, and both then gradually towards the bases. There was one from 2-5 mm. calcification in the spleen of a twenty year type. It was similar to the last case except the calcified caseation, resorption and water marking extended farther out towards the periphery. There were also two calcified lesions in the liver of a similar age character (Fig. 15*a*).

Comment. The evidence is all in favor of these lesions being tuberculous. An old ossified lesion in the right apex is compatible with an infection of over twenty years and corresponds to the age of the calcification in the spleen and liver. There was a gradual decrease in age characteristics of the calcified lesions in the lung from the apex towards the mid-field with more recent formations in the left upper and both bases.

Case xiv. C. N. (A1023), an American male, aged fifty at the time of death. There is nothing important in the early history. The disease began as a pleurisy in 1928. Death occurred nine years later.

There were multiple calcifications in the right base, up to the hilum, and the right side of the trachea. There were 18 calcifications in the spleen. The section shows them to be of the same age character, namely eighteen to twenty years (Fig. 15*b*).

Comment. The evidence is all in favor of tuberculosis.

Case xv. T. H. (A1145), an American male, aged fifty-two at death. He was a printer and worked with a tuberculous patient in 1915. He began to feel tired in 1917 when a diagnosis of tuberculosis was made. He lingered until 1938 and died, twenty-one years after a diagnosis and perhaps twenty-three years after infection (Fig. 15*c*).

There were many small calcifications in the lungs, liver, and spleen.

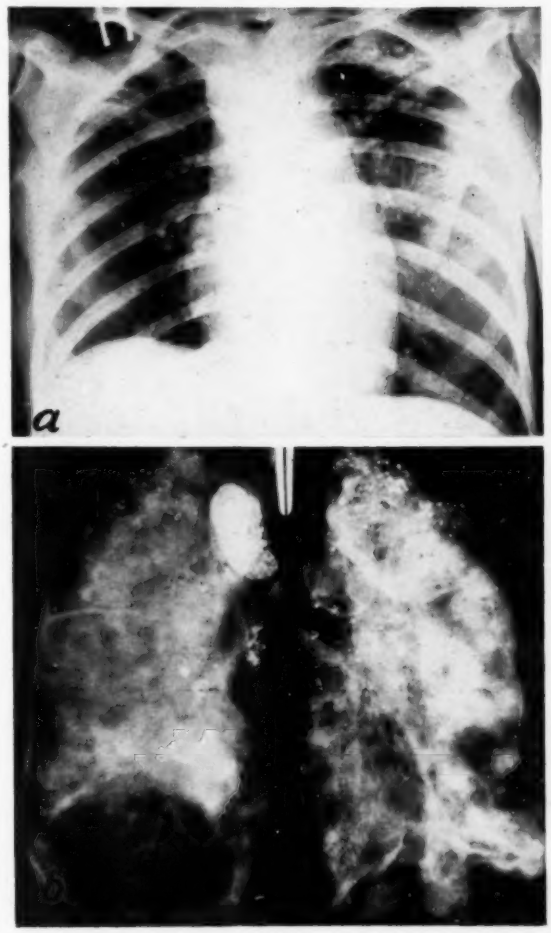

Fig. 12. *a*, antemortem roentgenogram of Case xi, taken October 30, 1936. *b*, postmortem roentgenogram of same, taken January 17, 1937. Note bilateral apical calcifications, hilum, and large paratracheal lymph node.

Comment. The history of contact corresponds favorably with the type and age of lesions found in the lungs, spleen and liver, which were of the twenty year type and suggest strongly a tuberculosis origin.

Case xvi. A. L. (A1066), male, aged forty-nine at death. There was nothing significant in his history except that his mother died of tuberculosis when he was six years old. The postmortem showed a typical exogenous reinfection type but there were old scattered calcified foci in the lungs and one in the spleen. Both were of great age and may represent a very old tuberculous process.

Comment. The lesion in the spleen would be classed as a phlebolith on roentgeno-

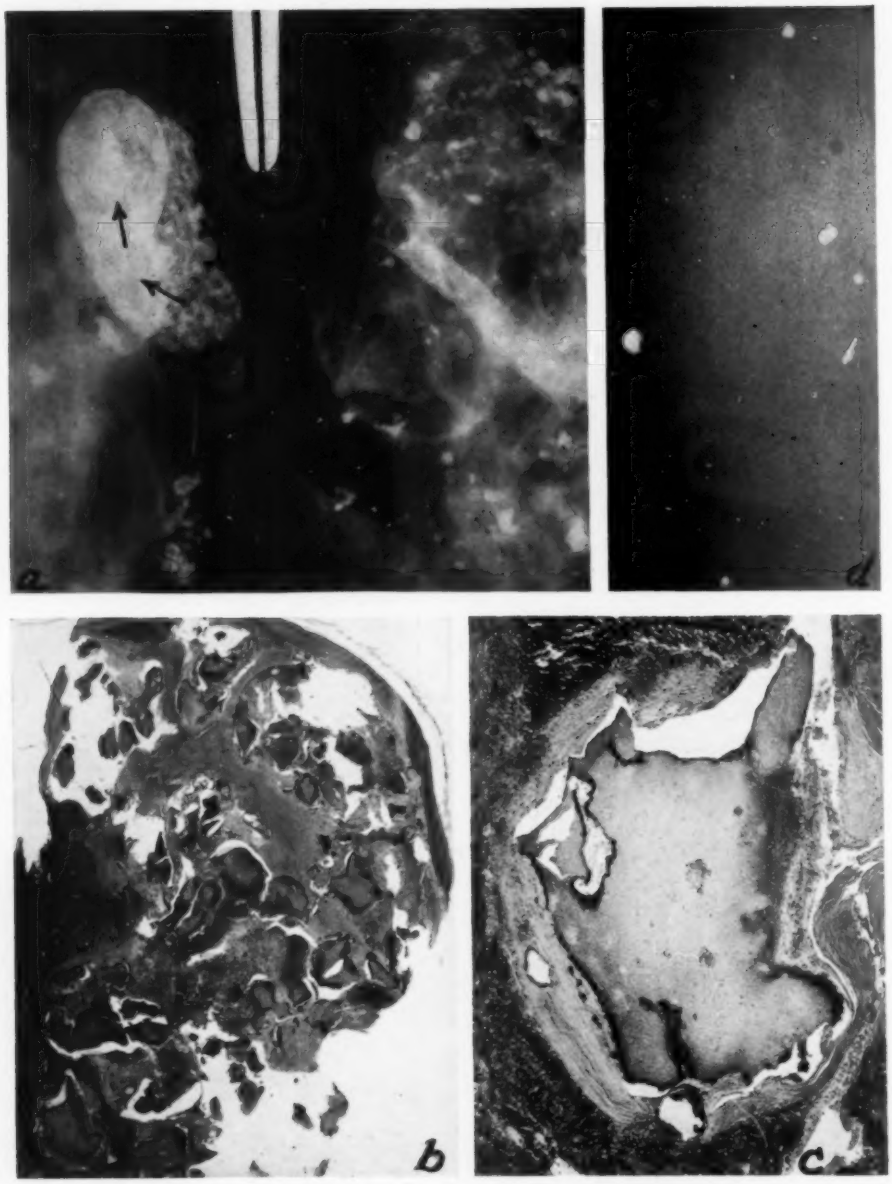

Fig. 13. *a*, enlarged section of hilum of Figure 12*a*. Note old hilar node and three ages to the paratracheal node. *b*, photomicrograph of section of hilar node. ×8.5. *c*, enlarged segment of *d*. ×45. (Hematoxylin and eosin.) *d*, postmortem roentgenogram of spleen showing calcifications. A twelve to fifteen year type.

logical examination and was compatible on microscopic study, but since it was similar in kind to those in the lung and corresponds to an old history of contact there is equal or more evidence in favor of its being a tubercle that had undergone an extreme degree of retrogression.

Case xvii. G. T. (A1193) was an American male, aged forty-six, with an uneventful history. His Wassermann reaction was positive. He was operated on for perinephric abscess seven months before death, and died of brain abscess following surgical removal of the kidney for kidney stone and abscess. There were twenty-four calcifications in the spleen and corresponding calcifications in the lung and lymph nodes of the same age character (Fig. 16*a* and *b*)

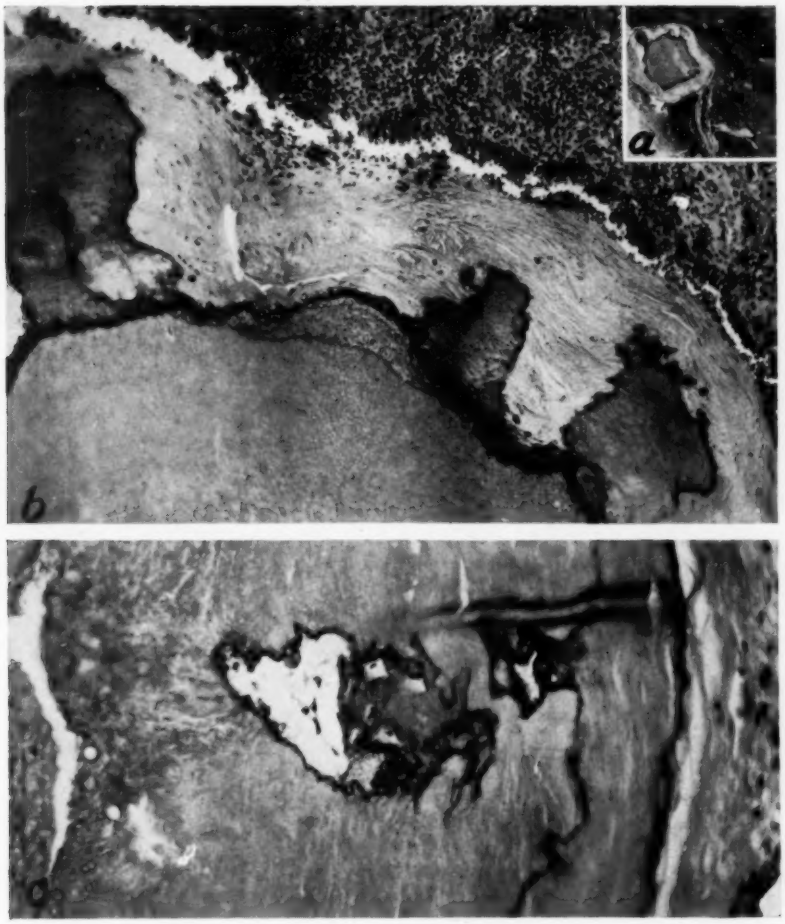

Fig. 14. *a*, low power photomicrograph of a spleen tubercle. ×8.5. *b*, section of capsule. ×134. Note "water marking." *c*, enlargement of section. ×290. (Hematoxylin and eosin.) Note beginning resorption and osteoid tissue. This is a twelve to fifteen year type.

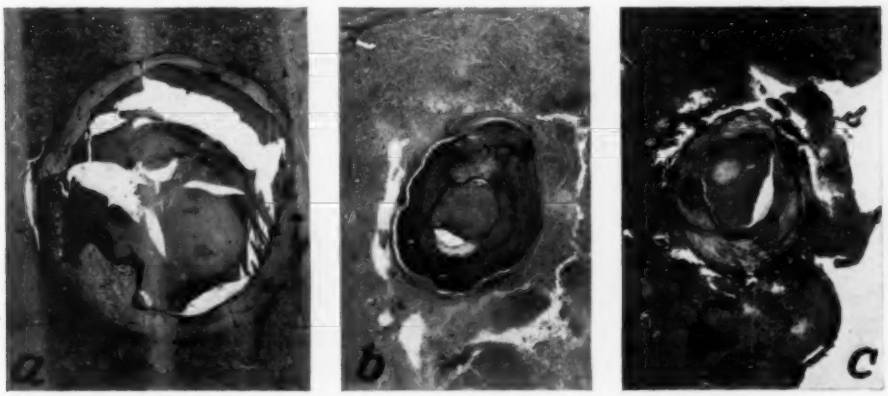

Fig. 15. Photomicrographs of sections of spleen. *a*, Case XIII showing "water marking" and resorption. *b*, Case XIV. *c*, Case XV. All of these are about the same general character and about the same age. They all had corresponding lesions in the lungs and lymph nodes. (All ×8.5; hematoxylin and eosin.) Twenty years or more in age.

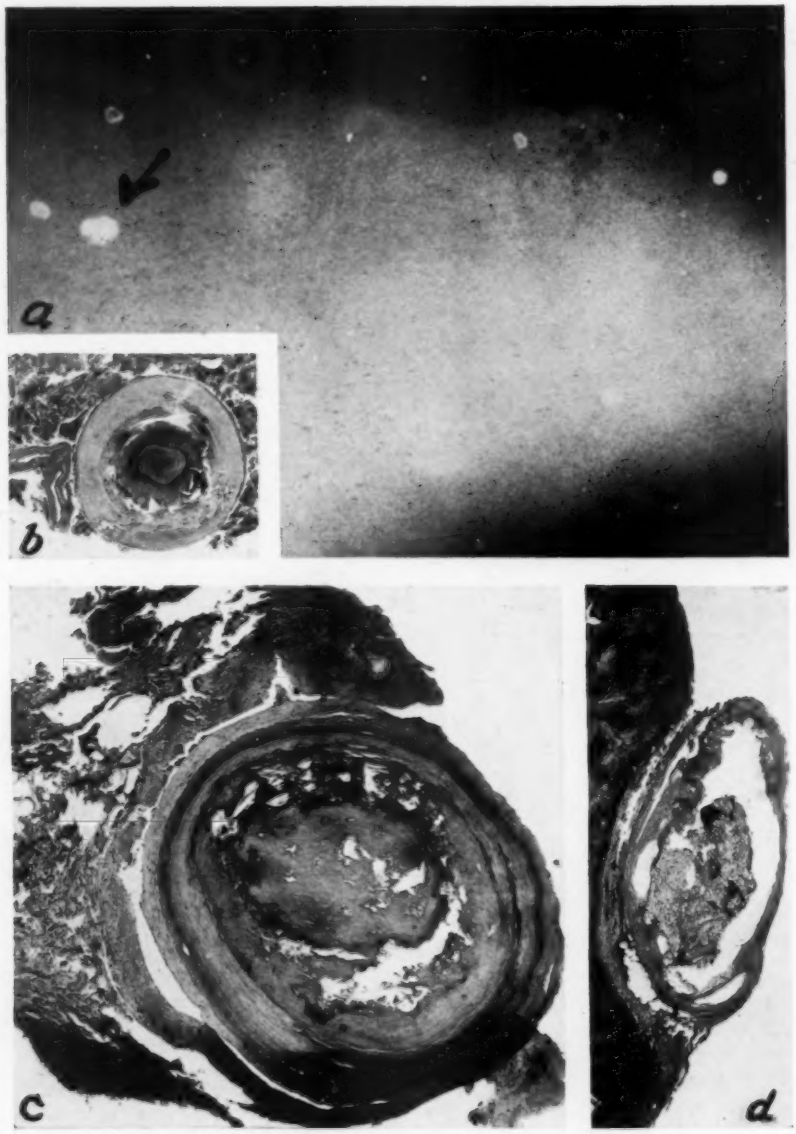

Fig. 16. *a*, postmortem roentgenogram of Case xviii. ×2.2. *b*, photomicrograph of one of the calcified lesions. This slightly resembles a phlebolith although there were similar lesions in the lungs and hilar lymph nodes. ×8.5. *c*, photomicrograph of phlebolith of another case, around the bladder. ×8.5. Note wall of vessel and central clot. *d*, photomicrograph of a calcified lipoma in the capsule of the liver. Note fat cells in the center. ×45. (All hematoxylin and eosin.)

Comment. The character of the splenic lesions is compatible with old phleboliths, and a history of syphilis makes this contention more plausible. Inasmuch as there is no absolute way to differentiate old phleboliths from very old tubercles, however, the cause must remain in doubt. These lesions are compared to others of a non-tuberculous origin (Fig. 16*c* and *d*).

Case xviii. J. A. W. (A931) was an American male, aged sixty at death in 1936. The essential features of his history were a pleurisy and a right sided rib resection at the age of ten. He was in contact with his father for one year, who died of tuberculosis in 1935. (Both no doubt had had the disease a long time.)

There was a very large calcified lymph node in the mesentery, and fifty-seven calcified nodules in the spleen. Both were very old. They

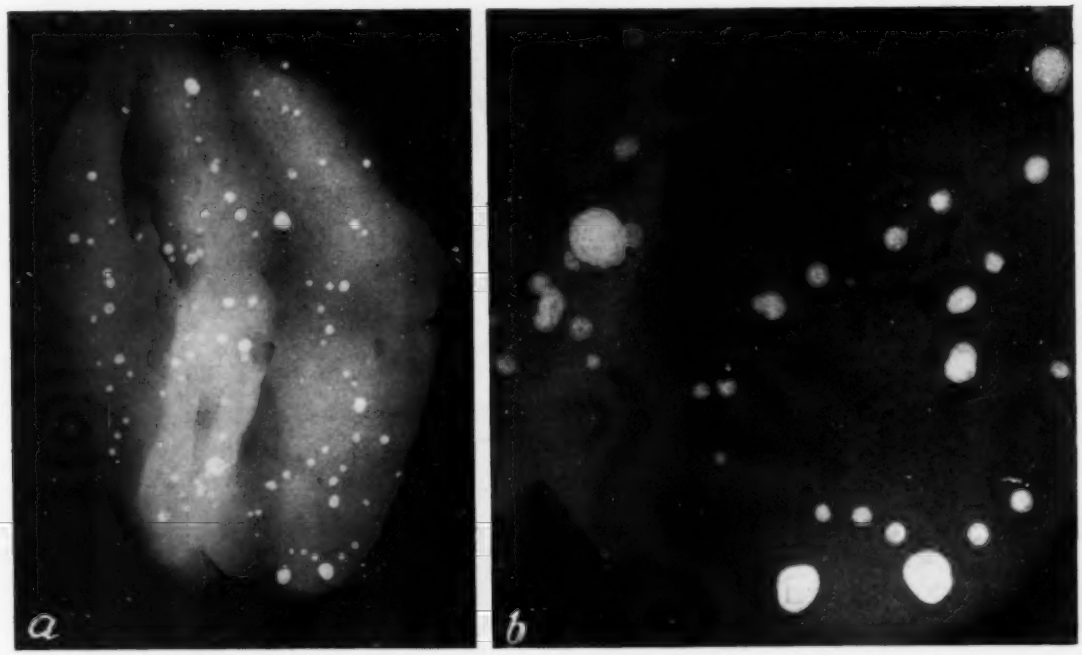

Fig. 17. *a*, postmortem roentgenogram of spleen of Case xx. *b*, enlarged segment showing resorption. There were corresponding calcifications in the lungs and lymph nodes.

may probably be of the same age. There were calcified lesions in the left lung but they may have been from hematogenous dissemination.

Comment. Even though these lesions were all very old the feeling is that the bulk of evidence is in favor of their tuberculous nature.

Case xix. J. M. H. (A1015) was an American male, aged fifty-one at death. There was nothing unusual in the history. There was a very old primary in the left mid-field and towards the hilum. There were two small calcified lesions in the spleen of the same age type.

Comment. As in the last case, tuberculosis cannot be ruled out.

Case xx. F. P. (A897) was an American male, aged sixty-one at death. He had a history of pneumonia when sixteen years of age. There was a large primary in the left base with an old calcification towards the hilum and a more recent calcification in relation to the left upper lobe. There were many calcified (105) lesions in the spleen measuring from 2-5 mm. in diameter.

Comment. They were compatible in age with the lung primary and this may have coincided with the pneumonia forty-five years before death. They resembled tubercles more than phleboliths in spite of the fact that the roentgenological diagnosis would perhaps have been the latter (Fig. 17*a* and *b*).

Discussion (Table 1)

This series of 20 cases, chosen more or less at random, is fairly representative of our material. The series represented practically all ages of spleen calcification, from a few months to fifty years old, 16 of which were in adults, and 18 were calcified.

Of this group there were 4 that were definitely tuberculous (2 not calcified). Four more had an exact correspondence of the age of the lesions, history, morphology, etc., and the ages of the lesions were all under ten years. There were 5 with a rough correspondence of the age of lesions, morphology, history, etc., but the history of the disease indicated an age of lesion between ten and twenty-three years. In 2 there was no correspondence at all, but due to an overwhelming tuberculosis else-

where and no other disease, it was probably tuberculosis by exclusion. In 4 cases of over twenty-five years' duration of tuberculosis there was a correspondence of history, lesions, etc., in 2, and a correspondence of lesions alone in 2, to make the lesions more compatible with a tuberculosis than anything else. In 1 case there was a correspondence of all the old calcified lesions, but there was a positive Wassermann reaction and the character of the lesions made them compatible with phleboliths, although a tuberculosis cannot be ruled out.

The series of tubercles described in the spleen and in the liver is so complete and consistent in progressive age characteristics and corresponds so well with old primary lesions found in the lungs, lymph nodes, liver, etc., that there is rarely left any doubt as to the tuberculous nature of the great majority of such lesions. They are easily accounted for as the hematogenous phase of the primary complex.

It is obvious that the age of the person has little to do with the character of the calcification. The age of the infection is more important. Where the infection is recent, irrespective of the age of the person, the findings are nearly always those of tuberculosis, and the lesions in the spleen correspond in age to those elsewhere. In only 1 case were there older lesions in the spleen than found in the lung and lymph node tubercles. It would be strange indeed for a large number of phleboliths to form only simultaneously with a primary tuberculosis complex.

In the very old infections also a corresponding primary tuberculous calcification can nearly always be found elsewhere in the body. Tuberculosis, therefore, can rarely ever be ruled out in any splenic calcification.

There is a consistent difference, however, between spleen tubercles and tubercles found elsewhere, in that typical bone is

Table I

Case Number	Age at Death (Years)	Approximate Age Infected	Maximum Age Tubercle, Lung	Maximum Age Tubercle, Lymph Node	Number of Calcified Tubercles in the Spleen	Maximum Age of Lesions in the Spleen	Capsule	Resorption	Number of Lesions in Liver	Maximum Age Tubercle, Liver	Cause of Spleen and Liver Lesions
I	1.1	0.8	0.8	0.8	Many	0.8	±	0	0	0	Tuberculosis
II	1.3	1.2	1.2	1.2	About 10	1.2	+	0	About 10	1	Tuberculosis
III	9.2	7	3	3	About 200 (6 calc.)	3	++	0	0	0	Tuberculosis (bacilli found)
IV	24.7	21	5	5	About 200 (7 calc.)	6	+++	0	0	0	Tuberculosis (bacilli found)
V	30.8	?	5	5	1	12	++++	++	0	0	Probably tuberculosis
VI	27.9	22	6	6	17	6	+++	0	0	0	Tuberculosis
VII	26.4	20	7	7	15	6	+++	0	0	0	Tuberculosis
VIII	19.6	13(?)	(?)	5	0	0	−	−	2	7	Probably tuberculosis
IX	10.5	1	10	10	15	10	++++	+	1	(?)	Tuberculosis
X	37.1	27(?)	10	10	12	10	++++	+	1	10	Tuberculosis
XI	23.5	8(?)	15	15	10	15	++++	++	0	0	Probably tuberculosis
XII	33.6	17	18	18	14	15	++++	++	0	0	Probably tuberculosis
XIII	29.3	8	20+	20+	1	18	++++	++	2	18	Probably tuberculosis
XIV	50.7	?	20+	20+	18	18	++++	++	0	0	Probably tuberculosis
XV	52.7	27	20+	20	100+	20+	++++	+++	10+	−	Probably tuberculosis
XVI	49.2	6	20+	20+	1	20+	++++	+++	4	−	More compatible with tuberculosis
XVII	46.0	?	20+	20+	24	20+	++++	+	0	0	More compatible with phleboliths
XVIII	60.0	50	G.-I. Lesion	20+	57	20+	++++	+++	0	0	More compatible with tuberculosis
XIX	51.8	?	20+	7+	2	12+	++++	+++	1	−	More compatible with tuberculosis
XX	61.0	45	20+	20+	105	20+	++++	+++	0	0	More compatible with tuberculosis

rarely ever found in the spleen. The fibroplastic cells that undergo a metaplasia to bone are apparently not so well developed or conditions for its development are lacking in the spleen. Otherwise the changes are similar, especially in the tubercles less than fifteen years of age. If anything, the spleen tubercles change more regularly but age a little more slowly than those elsewhere.

Some of the characteristics of these lesions will be detailed wherein they differ from other lesions in the body. After the tubercle forms there is the same progression observed during the early stages of development that have been described for tubercles elsewhere in the body. The central focus caseates, a nonspecific capsule forms, heavy specific fibers then form, and calcification begins to appear somewhere within the center, sometimes along the border of the capsule. The first calcification appears in about two years. There seems to be a slightly slower penetration of the calcium than in other tubercles. These foci are irregular in outline and remain so until the capsule is calcified. A heavy capsule appears in tubercles from four to seven years old and the central mass is rather well calcified, but rarely does the calcification appear as dense as it does in other tubercles. Sometimes the capsule may be seen on the postmortem roentgenogram as a halo around the calcified core. After ten years there is an overflowing of calcification into the heavy capsule and after twelve to fifteen years this calcification appears as a "water marking" in several places out towards the periphery. These water-marked areas show as bumps or bosses on the postmortem roentgenogram. At about the same time resorption appears in the center and sometimes the central mass is altered by large clefts of resorption. The same moth-eaten borders appear that have been described before for other tubercles. The "water marking" of calcifications may proceed until the whole capsule is involved when the roentgen shadow appears as a sphere with a central density having a surrounding moat. With few exceptions all of the very old specific calcifications show this phenomenon.

After fifteen or twenty years, therefore, there is little further change in the contour. but central clearing may be observed. The calcification in splenic tubercles may be compared to those in the lungs or lymph nodes where no bone has formed. In neither case can anything be said after fifteen or twenty years, and only the first ten years presents anything very definite.

These changes, on the whole, are so like those occurring in thoracic tubercles that there seems little doubt about their being tuberculous.

The study of nodules in the spleen from early caseous to fibrocaseous, calcareous and fibro-osteoid lesions have been so uniformly associated with tuberculous lesions elsewhere or so compatible with tuberculous lesions and so foreign to calcified lesions of other diseases that all but an insignificant minority seem to be tuberculous.

The argument sometimes advanced that tubercles only exist in children is fallacious. If calcifications are present in children, as universally admitted, and they do not become resorbed even in old age, why will they not be present also in the adult? Is not the "child the father of the man"? Furthermore, more of such lesions should be found in older people than in children because of the greater infection rate in the preceding generation.

SUMMARY AND CONCLUSIONS

1. A pathological-roentgenological study of the evolution of calcified lesions (principally in the spleen) has been carried out on a series of 20 tuberculous cases consisting of 16 adults and 4 children. Of these lesions, 16 had corresponding ages of lesions in the lungs, lymph nodes and spleen; 1 had corresponding lesions in the mesentery and spleen; 1 in the lungs, lymph nodes, liver and spleen; and in 2 there was no agreement of ages of the respective lesions.

2. The morphology of the lesions in the spleen undergoes a uniform evolutionary

development as the age of the lesion advances comparable to but not exactly like the changes previously reported for tubercles in the lungs and lymph nodes.

3. The spleen calcifications are rarely ever penetrated by capillaries but reveal an avascular type of resorption; they have rarely been found to show osteoid, marrow or lymphoid tissue; and as a result of the slow resorption of the "middle" capsule, the very old tubercles appear as perfect spheres.

4. In the majority of cases the lesions can be associated by age characteristics with a primary tuberculous infection elsewhere in the body and perhaps represent the hematogenous phase of it. This is true for all children and even for adults where there is evidence of a recent infection. Furthermore, as calcified lesions in the spleen apparently do not become resorbed, and as many have been found in old people that correspond to calcified lesions elsewhere, the assumption is justifiable that the majority of all such calcified lesions in the spleen are tubercles even in adults. This is all the more probable in old people, because in the past few generations the general infection rate was greater than it is today and more of such lesions should be found.

5. Phleboliths, although they may resemble tubercles in shape and size, are different in relation to associated lesions, in position, and in gross and microscopical appearance.

6. Small discrete calcified splenic lesions (in the Chicago area) caused by other diseases than tuberculosis are so scarce that for practical purposes they may be disregarded.

7. To insure greater accuracy, the roentgenological diagnosis of calcifications in the spleen should only be performed on good stereoroentgenograms; should be accompanied by a similar examination of the chest, neck, and lower abdomen for possible calcified tubercles, and should be interpreted in the light of a careful history of the patient for tuberculosis, splenic infarcts (endocarditis); cysts; hemorrhages; tropical fevers, etc.

8. The finding of calcified tubercles in the spleen has little clinical significance, *per se*, any more than to show that primary tuberculosis with hematogenous dissemination once existed and to help rule out other similar densities in the splenic region.

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PARADOXICAL ROENTGEN IMAGE IN PNEUMOTHORAX

A RESULT OF PACHYPLEURITIS

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INFLAMMATORY pleural thickening may be productive of numerous abnormal findings and distortion of the normal pulmonary markings in the chest roentgenogram. Individual effects are the result of the location and degree of pleural reaction in each instance. Chief emphasis has been placed in the literature upon the changes produced in this manner at the margins of the pulmonary area, that is, in the costal and diaphragmatic parietal pleurae, and upon the delineation of lobar outline by thickening of the pleural surfaces of the interlobar fissures. Thickening of the parietal pleura may be demonstrable as a rind-like pleural layer on the inner aspect of the lateral thoracic wall, where it shows as a crescent of diffuse density in the lateral extremity of the intercostal spaces as seen on the usual chest roentgenogram. Special roentgenographic technique has been developed to demonstrate this thickening with greater decisiveness.[3] The effect upon the diaphragmatic pleura may be demonstrated particularly in full inspiration in which position the obliteration of the costodiaphragmatic gutter by pleural adhesions is most notable, and the tenting of the diaphragm into the interlobar fissures is most accentuated. Confusion in the interpretation of unusual densities apparently in the pulmonary field has been in part avoided by an understanding of the extent and relationship of the interlobar fissures as demonstrated by their thickened pleural surfaces[4] and lateral and oblique positions have been developed to assist in more exact delineation of these boundaries.

A more unusual manifestation of pleural thickening as noted in the roentgenogram is that described as the paradoxical image of pneumothorax, or the opaque pneumothorax, description of which was apparently first offered by Torelli[5] in 1932 on the basis of 25 personally examined cases. In the discussion of these the author refers also to the views of Accorimboni[1] published in the same year. The paradoxical roentgen image of pneumothorax consists in the apparent reversal in the chest film of the densities of the area corresponding to the pneumothorax and of that representing the collapsed, or partially collapsed lung. Thus the usual picture of a partially collapsed lung shows peripherally an unusually penetrable area due to the medial retraction of the lung under the influence of the pneumothorax, and medially an area of increased density due to a corresponding condensation of pulmonary tissue against the mediastinum, principally in the region of the hilum. The latter area due to the atelectasis of the collapsed lung assumes a density to roentgen rays somewhat greater than that of the contralateral uncollapsed lung. An apparent reversal of this relationship of increased and decreased density in the roentgen picture of pneumothorax collapse is thus an unusual finding, and not a little disconcerting to interpretation at first view (Fig. 3).

Torelli considers that the reversal of apparent densities is due entirely to the increase in thickness of the costoparietal pleura of the pneumothorax space as a result of a pachypleuritis, or of diffuse fibrinous deposits on the parietal pleura, without involvement of the visceral pleura. The latter factor he considers indispensable to the formation of the paradoxical appearance under discussion. Thus a sharp margin will exist between the thickened and the normal pleura at the margin of ad-

hesion of the partially collapsed lung to the anterior or the posterior internal thoracic surfaces. This relationship is illustrated in Figure 1*A*, the heavy pleural line representing the thickened parietal pleura according to Torelli's concept and the line *ac* representing the uninvolved visceral pleura. It is thus apparent that in the lateral portion of the hemithorax the penetration of roentgen rays will be impeded by a double layer of thickened pleura, whereas in the medial portion of the chest only a single layer of thickened pleura will be thus interposed, the two areas being separated by a margin corresponding to the vertical projection of point *c*, and resulting in the reversal of the usual roentgen images. Accorimboni considered that the dense fibrinous deposits such as the "pleural mice" occasionally seen in pneumothorax collapse might account for such increased parietal density. The markedly uniform ground-glass appearance of the parietal area in the cases of opaque pneumothorax described in the literature and reported in the present paper is in contrast to the cumulus-like appearance to be expected with a density of such origin, judging by the usual picture of multiple "pleural mice." A uniformly distributed fibrinous deposit on the parietal pleura might as easily account for the findings, however, as a fibrous pleuritis, and the two may coexist as suggested by Torelli. The fibrinous character of such density could account by its later absorption for the reversion to the normal relationship of the affected areas in one instance noted by Torelli. He himself, however, considered the change due to an extension of the pachypleuritis to the visceral pleura which thus rendered the entire pneumothorax equally blanketed by thickened pleura, and obliterated the paradoxical image.

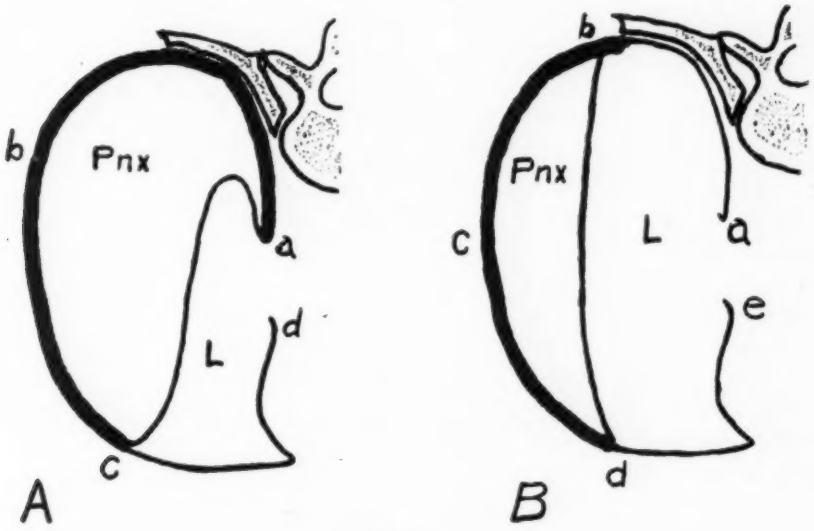

Fig. 1

A second possible explanation of the reversal of such densities in the roentgenogram in pneumothorax was offered by Zorini, quoted by Torelli, who demonstrated at autopsy the dissection of air between the layers of parietal pleura, producing a localized pneumothorax offering the impression of decreased density in the central zone of the pulmonary shadow. This mechanism would, of course, be unusual.

Opaque pneumothorax has also been reported by Berthet[2] who suggested that its genesis consisted in the re-expansion of a part of the lung adherent to the chest wall in the course of a pachypleuritis complicating pneumothorax. The lateral

migration of the line between areas of increased and decreased density as noted between Figures 3 and 4 of the present case report could then be due to the separation of the already thickened pleura from its costal attachment by the advancing pulmonary alveoli, or by the contraction of the fibrosing pleura. It is, of course, obviously necessary that the coherent areas of visceral and parietal pleura be themselves unthickened.

The production of the paradoxical roentgen images under discussion could be produced, however, by a mechanism in addition to those suggested by Torelli, Berthet, and Zorini, and illustrated in Figure 1*B*. Thus, if the lung *L* be adherent to both anterior and posterior walls at *b* and *d* with unthickened coherent visceral and parietal pleura *ab* and *de*, and with thickened parietal pleura *bcd*, the passage of roentgen rays through the chest would be more impeded in the lateral than in the medial portion of the hemithorax, thus giving rise to the paradoxical roentgen image. This would be entirely independent of thickening of the non-adherent portion of visceral pleura *bd*. This concept would be particularly useful in the present case report where lines suggestive of thickening of the free visceral pleura are demonstrable and intrathoracic pressure changes were such as to suggest uniform thickening of all walls of the pneumothorax cavity.

It would thus appear by reference to Figure 1 that the essential condition for the occurrence of this interesting relationship of densities will include the following:

(1) A partial pulmonary collapse by pneumothorax with adhesion of the lung to both the anterior and posterior wall in case of thickening of the visceral pleura (Fig. 1*B*) or to either wall in case the visceral pleura is not thickened (Fig. 1*A*). Adhesion to both anterior and posterior walls would, of course, be possible without thickening of the visceral pleura, but it is obvious that adhesions to but one wall in case of thickening of the visceral pleura would interpose between the tube and the screen an identical number of thickened pleural surfaces over both air and lung containing areas of the pneumothorax. As a result no margination could occur and the entire hemithorax could show only the ground-glass increase in density.

(2) A diffuse thickening of the non-adherent parietal pleura, or the uniform deposit of fibrin upon its inner surface with or without the extension of this process to the exposed visceral pleura according to the conditions in (1).

(3) Absence of pleural thickening under the adherent areas of the lung.

CASE REPORT

The following instance of opaque pneumothorax, or pneumothorax with paradoxical roentgen appearance, is offered in illustration of the entity thus discussed and to facilitate its better understanding.

H. D., aged twenty-two, white, unmarried, female, typist, was given pneumothorax collapse of the right lung September 1–7, 1936, in treatment of moderately advanced pulmonary tuberculosis with a 3 cm. cavity in the apex of the right lower lobe, and a slight bronchogenic mid-lung spread to the left lung. Sputum had been repeatedly positive and progress of the disease had been intermittent despite partial bed rest during the previous year. Collapse was achieved without incident, but was complicated by broad apical and basilar adhesions and by a narrow mid-lung adhesion which did not appear to interfere with adequate collapse of the affected area. Pneumothorax was therefore continued, but the patient remained febrile, and one month after initial collapse increased physical signs were noted over the left lower lobe. A roentgenogram two months after beginning collapse (Fig. 2) showed no increase in demonstrable infiltration in the left lung, but a slight exudate in the right pleural cavity. Pneumothorax refills changed quickly at this time from the weekly injection of 400–600 cc. with negative terminal pressures to the injection of 100–150 cc. with the attain-

ment of high positive pleural pressure. Fluid remained minimal and sterile to culture and guinea-pig inoculation. Clinical improvement occurred soon thereafter with weight gain and a diminished febrile course. Roentgenogram seven months after initial collapse (Fig. 3) showed typical paradoxical pneumothorax densities with apparent absence of cavitation

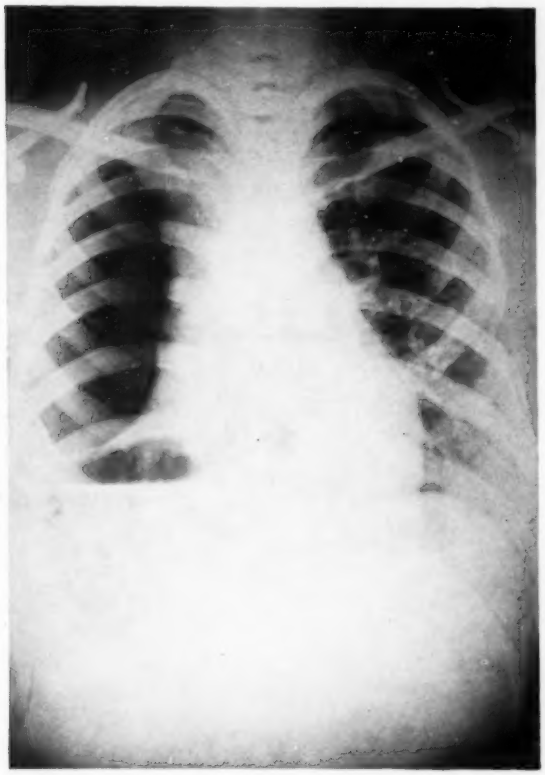

Fig. 2. Roentgenogram of the chest showing right hydropneumothorax with broad apical and basilar, and narrow mid-lung adhesions.

in the right lung, and disappearance of all pleural fluid. All former adhesions appeared to have vanished except a part of that to the diaphragm. No clinical episode had suggested the separation of these bands, though such may have been responsible for the pleural effusion.

General clinical improvement continued with complete absence of fever, a gain in weight, increased physical activity, and maintenance of an intrapleural pressure between +5 and +10 cm. of water by weekly refills. By this means it was hoped to delay the expansion of the collapsed lung. The patient returned to full physical activity within thirteen months after

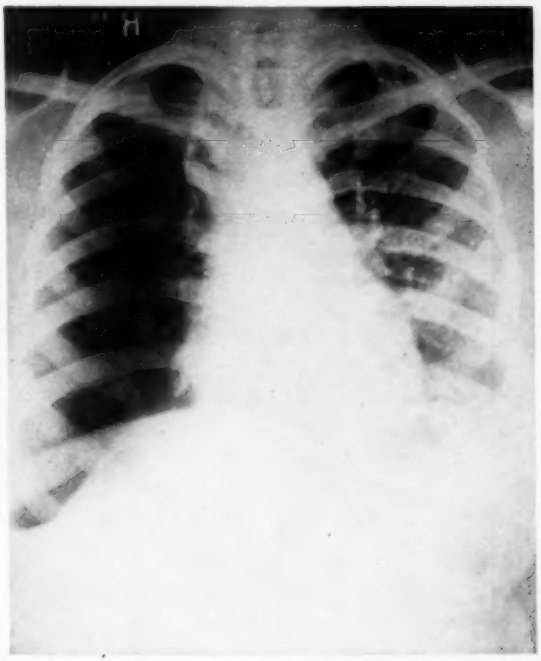

Fig. 3. Roentgenogram four months after Figure 2, showing paradoxical image of pneumothorax collapse, with disappearance of adhesions.

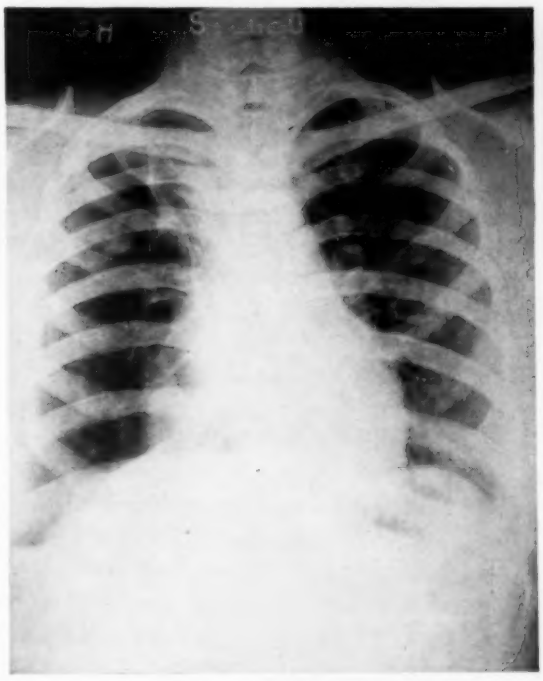

Fig. 4. Roentgenogram seven months after Figure 3, showing lateral migration of lung border with persistence of paradoxical image, and greater prominence of apical and basilar adhesions. The lower half of the border between the greater and lesser distances is now condensed to a line suggesting pachypleuritis.

beginning pneumothorax, and to part time employment after fifteen months. A roentgenogram at this time (Fig. 4) showed increasing expansion of the right lung with maintenance of the opacity of the pneumothorax area. The diaphragmatic adhesion had appeared to become broader, and apical adhesion was again apparent. In the lower half of the margin between areas of increased and decreased density between the lung and pneumothorax, the visceral pleura appeared condensed to a slightly prominent line, not apparent upon the previous film, and suggestive of the thickening of the visceral pleura. Unchanged relationships were maintained on a film twenty-eight months after beginning pneumothorax except for slightly greater expansion of the lung area. The patient meanwhile had returned to full time occupation.

Comment. Inspection of Figures 3 and 4 show the typical picture of paradoxical roentgen images in pneumothorax described by Torelli and Berthet. The diffuse, uniform consistency of the ground-glass-like peripheral density discourages belief in the accumulation of fibrinous "pleural mice" as the cause of the density and lends credence to its causation by a diffuse pachymeningitis or uniform fibrinous deposits. In view of the demonstration of thickening of the visceral pleura in Figure 4, we are unable to agree with Torelli that an intact visceral pleura is essential to the formation of the opaque pneumothorax, and offer an explanation in Figure 1*B* for the occurrence of the roentgen findings despite thickened visceral pleura. The disappearance of adhesions apparent in Figure 2 is probably ascribed to their separation which may have been causative of the acute effusion; it is unlikely that they could be concealed by such slight density of the peripheral pleura. It is further noted that the lung fields of the collapsed lung in Figures 3 and 4 are distinctly less dense than seen at even the periphery of the left uncollapsed lung. It would appear probable that this apparent increased penetrability, otherwise associated with an emphysema, would depend upon the penetration of this peripheral portion of the lung by roentgen rays which were not forced to traverse also a large mass of extrathoracic tissue, such as is done by the rays tangent to the lateral wall of the chest. The marked diminution in size of pneumothorax refills and the inflexibility of intrapleural volume as reflected by the rapid attainment of positive pressure are further suggestive of a pachypleuritis as a cause of the changes noted in the roentgenogram. It is to be doubted if such pressure and volume data could pertain without thickening of the visceral as well as the parietal layers of the pleura.

SUMMARY

The concept of "opaque pneumothorax" or paradoxical roentgen images in pneumothorax is presented, and its pathogenesis is discussed. A case history is presented supporting the contention that the visceral pleura may or may not be involved in the diffuse pachypleuritis responsible for the roentgen appearance of the increased peripheral and decreased central densities in the hemithorax demonstrating these unusual roentgen appearances. The occurrences of this complication did not interfere with the successful conclusion of the case presented, by continuation of pneumothorax.

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Vol. 44, No. 2

THE DELETERIOUS EFFECTS OF DEEP ROENTGEN IRRADIATION ON LUNG STRUCTURE AND FUNCTION*

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THE effects of roentgen rays on animal tissues are well known in many respects, but new facts are being added from time to time, an indication that there are frontiers yet to be explored. This is to be expected, since the penetrability of the rays, the exposure time, and other factors are frequently altered in the quest of better delineation of internal organs or—and this is very important at present—in the effort to destroy neoplastic disease. Radiotherapy constitutes a large chapter in modern therapeutics, as a part of the great fight against cancer—in which all arms of the service are invoked.

There is probably no variety of neoplasm which has not been subjected to roentgen and radium rays, but the types which succumb to such treatment are unfortunately few. Some tumors have been aroused to more rapid growth by these rays, but pathologists and roentgenologists by combining their skills are able to foretell, with a fair degree of accuracy, that certain tumors will be destroyed, certain others inhibited, that a large group will in all probability be uninfluenced in the slightest degree, and some positively increased in virulence by irradiation. What may be a killing dose at the periphery of a tumor may be toned down to a stimulating dose in its center by the simple presence of matter in the form of neoplastic cells or normal cells, dead or alive. All these tissue elements act as targets for the production of electrons or cathode rays, which by their scattering effect are less controllable in the depths of animal tissue.

Johannes Müller first enunciated the truth that all tumors are derived from the tissues of the host. It is natural then that the non-neoplastic body cells, united as they are to form a variety of organs of many different degrees of density, react to roentgen rays qualitatively about as do tumor cells. Quantitatively, they exhibit more resistance as a rule, but there are striking examples of normal structures, such as lymphoid tissue and germinal epithelium, being much more radiosensitive than most malignant tumors. The great ubiquity of lymphoid tissue provides a widespread distribution of potential foci foy lymphoid tumors *de novo*, and justifies more often than not treatment by irradiation of "tumors" whose existence may or may not have been first proved by biopsy.

The benign tumors encountered in the young generally follow in their amenability to treatment the course of similar benign tumors in later life, but the malignant tumors of youth achieve a great momentum, the virulence of youth, and the main tumors of this group which are very radiosensitive are of either lymphoid or primitive epithelial origin. In the "cancer age" epithelial tumors predominate and, since they usually show more differentiation, are more resistant to radiotherapy (law of Bergonié and Tribondeau). However, many such neoplasms are in locations not suitable for radical surgery, or need preliminary irradiation of an infiltrated area preparatory to surgery. Destruction of some of these growths by irradiation has been achieved in every properly equipped institution, and much relief is often possible even though five year cures are few. Thus in considering the therapeusis to be used in the treatment of neoplasms of in-

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ternal organs essential to life, such as the lung, the non-surgical method—radiotherapy—must be accorded first place.

In the days of low voltage limits and hence of low penetration, there was little to offer the patient suffering from cancer of the lung or retroperitoneal tissues. The vast strides of recent years in increasing the voltage of roentgen machines and the improvement of all phases of roentgen irradiation methods have widened the field of radiotherapy so that tumors heretofore regarded as hopelessly inaccessible are being attacked vigorously and with increasing chance of success. The radium "bomb" can be considered at the same time, and it is not the purpose of this paper to argue for or against these two sources of penetrating rays. Both have their places of greatest service, although for the deepest penetration over a wide area roentgen rays at present seem preferable.

This paper is concerned chiefly with the reasons usually invoked for the pursuance of a program of deep roentgen treatment of a suspected tumor of the lung—the justification of such a program by experience with lymphoid and epithelial tumors of that organ.

The medical literature of recent years shows a steady increase in the recognition of important by-effects of deep roentgen irradiation on the structure and function of lungs, the seat of primary or secondary neoplasms. The pathological changes recorded are becoming of more constant pattern, but the evidence presented has usually been visible only in roentgenograms. Very rarely has there been available for anatomical study the lung itself from a patient regarded as having suffered at one time or another from the effects of irradiation in previously normal or relatively normal lungs. That is why I feel that the following presentation is of interest, as it includes a postmortem study of a man, probably the second on record, who was diagnosed clinically as having a cancer of the lung, subjected to deep roentgen therapy over a period of nine years, and whose death was undoubtedly the result of the radiotherapy and not directly due to the neoplasm.

HISTORY OF CASE

The patient was a white male, aged forty-six. He was with the A.E.F. in France, and attached to the British Army at Amiens. He had had slight contact with mustard gas, but was never invalided by it. He had been subject to colds all his life and suffered a mild attack of epidemic influenza in France in 1918.

In 1922 he developed pains in his chest with some cough, and at the Memorial Hospital in New York in 1923, a tentative diagnosis of pulmonary tuberculosis or Hodgkin's disease was made. The latter possibility was considered more likely, and in October, 1923, he had a course of deep roentgen treatment in fractionated doses, altogether about 2,500 r.

In the winter of 1924, there was a considerable increase in coughing and a marked hemoptysis following a cold. He spent the following year at Saranac Lake under the care of Dr. Lawrason Brown. A diagnosis was made of bronchiectasis. He had one episode there of a hemoptysis of about one quart. In January, 1924, just previous to going to Saranac, he was again irradiated with 2,000 r, and during the subsequent nine years he received six other courses of deep roentgen irradiation, the last one in September, 1933, altogether approximately 18,300 r. Most of the treatments were with 200 kv., 50 cm. distance, filter 0.5 mm. copper, 5 ma., eight to thirty minute exposures over two to four different portals.

In November, 1925, he was at Mt. Sinai Hospital in New York, where a bronchoscopic examination was made and a piece of tissue removed from the right bronchus. This showed only normal bronchial mucosa. While there, he had some pains in the left hip, and a few roentgen treatments of that hip relieved the pain.

Ever since 1922, he had been short of breath, and on exertion dyspnea would occur. This would be followed by a racking cough with at times considerable sputum, frequently blood-tinged. His voice would become husky during these episodes. There had been considerable expectoration in the morning for the past thirteen years, but without any conspicuously foul odor.

In 1927 he had a large pulmonary hemorrhage, losing about a quart of blood. He had had one similar experience while at Saranac

Lake in 1924. Sputum had always been negative for acid fast bacilli, and the flora quite mixed at all times. His maximum weight was 154 pounds, but he maintained a steady average of 145 pounds for the last ten years of his life.

In 1935 he had an attack of bronchopneumonia in Florida with a temperature of 104° F. for one week. His energy had been greatly diminished since then, and he was of the opinion that there was some fever most of the time.

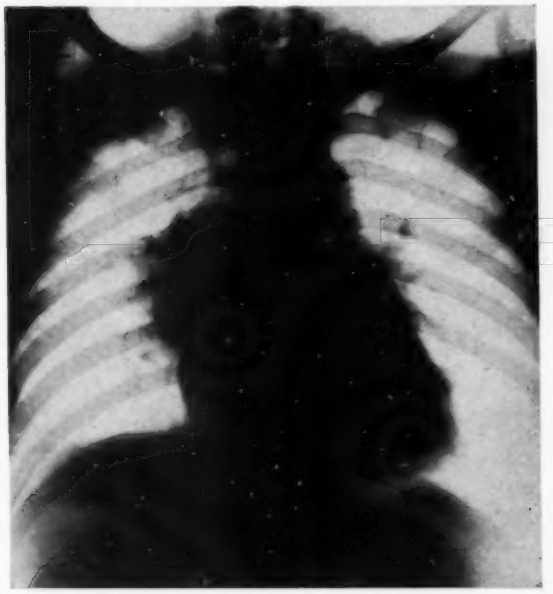

Fig. 1. Roentgenogram of chest in 1923. At right hilum a dense shadow considered then either tuberculosis or Hodgkin's disease.

There had been no disturbance of heart action, no palpitation or edema. He slept poorly, requiring mild sedatives most of the time. He used one pillow. He tired easily on walking, and pain across the chest with some cough developed along with the fatigue. Appetite was poor for several weeks at a time. Bowels were normal until his last illness. Frequent spells of nausea occurred without vomiting.

Family History. Married; wife is an arrested case of pulmonary tuberculosis. Mother died of tuberculosis at Saranac Lake.

Physical Examination. Well developed and nourished, male white adult. Weight 149 pounds; height 67⅛ inches. Neurological examination normal. Finger nails were rounded, but there was no definite clubbing.

Fig. 2. In 1924 after a course of deep roentgen therapy of unknown amount. A slight decrease in size of the right hilar shadow over that of 1923, also beginning elevation of the right wing of the diaphragm.

The expansion of the right lung was much restricted. The lower two-thirds had a high pitched dull note to percussion, with increased

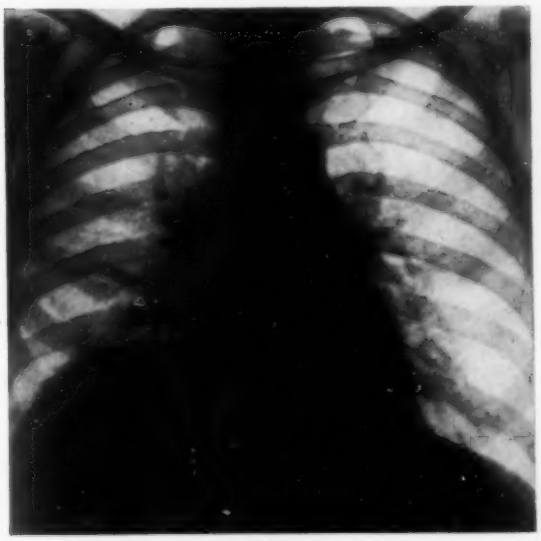

Fig. 3. In 1926, after two further courses of deep roentgen therapy. The hilar shadow is still smaller, but there is peribronchial infiltration on both sides and marked elevation of the right wing of the diaphragm.

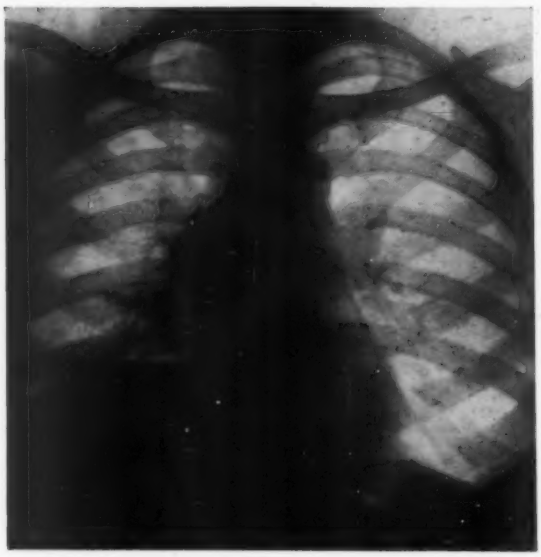

Fig. 4. In 1927, the right hilar shadow is very dense, but well circumscribed. Fibrotic changes are present leading out into the parenchyma. The pericardium is pulled slightly to the right.

tactile and vocal fremitus. Cog-wheel breathing over the upper two-thirds of the right scapula. Over the anterior upper third a few coarse inspiratory râles. Breathing was of slightly amphoric quality posteriorly. Left lung showed evidence of marked emphysema, but few râles.

The cardiac margins were obscured by emphysema. Action regular. No murmurs. P_2 not accentuated. Right border merged with the dullness of the right lung. Some contraction of the right apex. No enlarged glands in the neck. Blood pressure 116/90. Vital capacity 1,800 cc.

Laboratory Findings. Hemoglobin 102 per cent. Red blood cells 4,840,000; white cells, 7,200. Blood Wassermann negative.

Blood differential—polymorphonuclears, 71 per cent; lymphocytes, 22 per cent; monocytes, 5 per cent; eosinophils, 1 per cent; basophils, 1 per cent; platelets and red blood cells normal.

Urine contained albumin and many granular and cellular casts.

Roentgenoscopic Examination. Large shadow in right lung involving lower and middle lobes and densest at the hilum. Peribronchial thickening in upper lobe. Right apex clear. Left lung showed peribronchial thickening in region of hilum.

Sputum Examination. Many white blood cells; many polymorphonuclears; pneumococci; streptococci and mycelia resembling streptothrix. Fixed specimen showed no cancer cells or spirilla. Tubercle bacilli were never found in many examinations. The streptothrix was not constant.

Course. Between 1935 and June, 1937, he had frequent episodes of acute bronchitis with massive hemoptysis, but each time he would recover and the blood approached normal. No significant loss of weight. There was, however, marked loss of strength after each attack and this was never entirely regained. Temperature of 99°F. in the afternoon was very common, but during acute pulmonary infections it would reach 101° F. He was in the Samaritan Hospital, Troy, New York, several times with such incidents.

In 1936 severe sciatic pain in his left leg associated with herpes zoster of the left buttock finally necessitated injection of the sciatic nerve by alcohol. This was done by Dr. Peter Harvie on September 16 with slight relief. It was repeated September 25 with much better results. He subsequently developed a foot drop on that side and some atrophy of the tibial muscles. At that time it was considered that he might have metastasis in the region of the exit of the sciatic nerve through the sciatic foramen.

Roentgenograms of the lung were taken sev-

Fig. 5. In 1931, after several further courses of roentgen therapy the right lung shows some increase in size of the hilar shadow. The diaphragm on the right is higher than before. An increase in density is seen in the lower lobe as well and in less degree in the left lung. The right intercostal spaces are narrower than those on the left.

eral times during these years and they will be discussed in more detail later. In March, 1937, hemoglobin was 91 per cent. In June following a severe hemorrhage, hemoglobin dropped to 85 per cent. Blood pressure remained normal. Thromboplastin injections seemed to help control the bleeding which generally stopped in about a week. On June 18, his hemoglobin had dropped to 60 per cent; red cells 3,800,000; blood pressure 130/78; pulse 104. For the past two years his pulse had been consistently high, from 90–120, but regular. A few myelocytes were present in the blood with white count around 8,000. Because of the history and physical findings it was felt that if there was a tumor in the lung, it must be a very benign one, but prone to hemorrhage. Teratoma and hemangioma were considered, and while roentgen irradiation had been of some benefit at times in controlling the hemorrhage, the secondary constitutional effects had been such that it was thought advisable not to try it again.

In September, 1937, he had a period of hemoptysis lasting three weeks. Thromboplastin was of no help at this time. His hemoglobin dropped to 64 per cent; white blood cells 7,400;

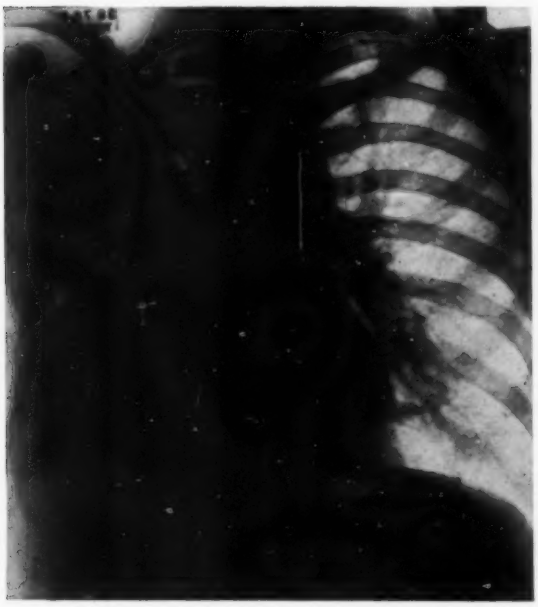

Fig. 6. In 1937, the right lung contains very little air-containing tissue. A dense fibrosing process obscures the diaphragm level on the right. The pericardium is further retracted to the right. Peribronchial thickening marked at left hilum and spreading into left lower lobe.

Fig. 7. In 1938, a lipiodol injection by Dr. G. Oberrender, Lenox Hill Hospital, New York, shows the passage of the lipiodol into the right middle and lower lobes, but with very little evidence of bronchiectasis.

red blood cells 4,900,000; 79 per cent polymorphonuclears with a marked shift to the left; a few myelocytes. He was referred to Dr. H. McLeod Riggins of New York who studied him very thoroughly. Bronchoscopic examinations and lipiodol injections were made by Dr. Girard F. Oberrender.

He improved subjectively to a great degree following these administrations. Weight came up from 148 to 157 pounds in about three weeks. Hemoglobin rose to 90 per cent; blood pressure 118/82; pulse averaged around 104.

He returned to New York October 27 where Dr. Oberrender performed a bronchoscopy and removed much mucus from the bronchi. The cough was greatly diminished, and where there had previously been widespread râles throughout the right chest, there were very few at this time. Hemoglobin rose to 93 per cent.

On November 10 he had hemoptysis, following a coughing spell, which lasted twelve hours. Diarrhea recurred. Cough increased in amount and he developed pains and considerable tenderness over the costovertebral angles. Temperature 101° F; pulse 120.

He attended a Christmas party which proved to be a strenuous effort for him. On January 2, 1938, he had a severe chill with vomiting. The urine was highly colored; contained a trace of

Fig. 8. The right lung, anterior view, converted into a mass the size of a man's fist. The pleura is 2–4 mm. thick, pearly white and very hard. At the left is a piece of fused parietal and visceral pleura stripped from the lung, showing rib markings and prominent blood vessels.

albumin, many leukocytes, singly and in clumps; many hyaline and granular casts. He developed no peripheral edema, but blood nonprotein nitrogen was 48.3 milligrams per 100 cc. Hemoglobin 85 per cent; red blood cells 4,900,000; white blood cells 7,400.

He was taken to the Samaritan Hospital, Troy, New York, where he continued to decline, becoming progressively weaker, with considerable cough and frequent hemoptysis. He died on January 8, 1938.

Anatomical Diagnoses. (1) lobar pneumonia, left; (2) perinephric abscess, left; (3) abscesses of kidneys; (4) old fibrous pneumonitis, right, with atelectasis; (5) chronic adhesive pleuritis, right; (6) acute splenitis; (7) eburnation of rib cortex (right chest) due to exposure to roentgen rays.

Historical Landmarks. (1) pericardial adhesions; (2) healed mitral valvular endocarditis.

Microscopical Diagnoses. (1) adenocarcinoma of right bronchus; (2) irradiation pleuropulmonitis; (3) acute bronchopneumonia, bilateral; (4) perinephric abscess, left; (5) abscess of left kidney; (6) septicemia; (7) acute myocarditis.

Body: A well developed and nourished male white adult, 67 inches in length. Rigor mortis and postmortem lividity present. Lips and finger tips cyanotic. Pupils contracted. Skin over right chest denuded of hair and superficial capillaries are dilated (old roentgen effect). Finger nails definitely curved.

Primary Incision: About 1.5 cm. of yellow subcutaneous fat. Skin over right chest moderately thickened. Pectoral muscles appear normal. In removing the sternum, it is found that the rib cortex of the right chest is about four times normal thickness, reducing the rib marrow space to very small proportions. The left ribs cut easily and the marrow is red and of normal amount.

Diaphragm: On the right is level with the third interspace, on the left with the fourth interspace.

Pleural Cavities: The right is obliterated by fibrous adhesions which are densest anteriorly and so adherent that a portion of the lung substance is left attached to chest wall after cutting it loose. The striking feature is the small size of the pleural space due to the fact that the

Fig. 9. Right lung opened by frontal section, posterior view. Pleura forms thick fibrous encasement. Interstitial fibrosis, atelectasis, areas of emphysema, and congestion are shown. Also a granular productive inflammation of trachea, bronchi, and bronchioles. The diaphragm is adherent. Lymph nodes slightly enlarged from edema and mild inflammatory changes. No tumor visible in this view.

right lung is reduced to the size of a medium-sized grapefruit.

The left pleural cavity shows a few fibrous adhesions on diaphragmatic surface. Fibrinous adhesions diffusely scattered over almost entire pleural surface.

Mediastinum: The pericardial sac is pulled slightly to the right being fused with parietal and visceral pleurae. The lymph nodes are

Fig. 10. Right lung, frontal section, posterior to view in Figure 9. The arrow points to the remnant of the adenocarcinoma which is in communication with the extrapulmonary portion of the right bronchus. The tumor has a viable, dark periphery and necrotic center. Just above it are several pools of mucus which had been sealed off from the lumen, probably in the manner of acquired diverticula. Purulent bronchitis and bronchiectasis in the larger tubes with lumen narrowed by granulation tissue. Thrombosis of pulmonary veins has also occurred. The thick pleura and interstitial fibrosis are well shown.

moderately enlarged, edematous, congested and anthracotic. The thymus is atrophic and the fat is in normal amount.

Pericardial Sac: Contains about 50 cc. of clear, pale yellow fluid. Numerous fibrous adhesions on upper anterior surface and a few at base posteriorly.

Heart: Weighs 350 grams; auricles slightly dilated; ventricles normal size. Right ventricle wall moderately increased in thickness. A slight degree of healed mitral endocarditis.

Right Lung: Weighs 725 grams. Except for a region about 3 cm. in thickness at the apex, it is of dense fibrous consistence throughout. Pleura anteriorly about 3 mm. thick and very dense.

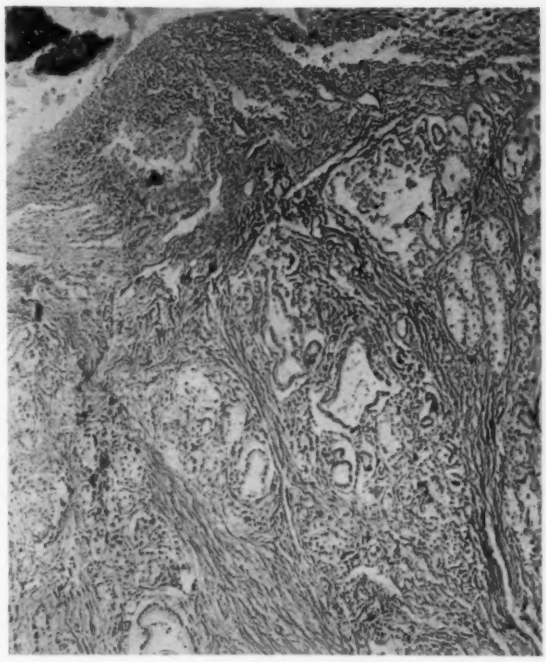

Fig. 11. Photomicrograph of the tumor. Upper surface necrotic. Lower two-thirds shows typical adenocarcinoma with invasion of the stroma by atypical glandular structures.

Posteriorly it is also thickened, but much less than anteriorly. On section it cuts with greatly increased resistance. Considerable anthracosis present and a diffuse scarring seems to have occurred. Bronchioles are dilated in the middle portion, but there is very little true bronchiectasis present.

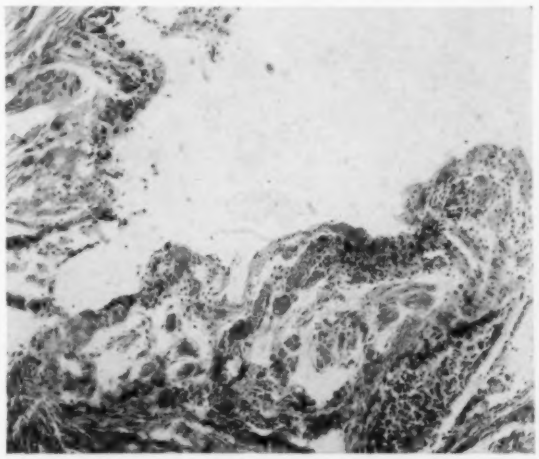

Fig. 12. The mucosa of a branch of the right bronchus showing loss of epithelial lining and vascular granulations with superficial capillary hemorrhages.

After fixing the lung for several weeks in 10 per cent formalin, it was cut in frontal serial sections. The right primary bronchus except for a portion of the anterior aspect is embedded in very dense opaque white tissue of the consistence of old scar tissue. There are several anthracotic lymph nodes, moderately enlarged, in this mass. Also, about 1 cm. from the wall of the bronchus and connected with it by a narrow tongue of friable tissue is a mass 2×2×1 cm. with a grayish white soft centrum and slightly anthracotic, firmer periphery. This is located about 2 cm. from the hilum. The middle lobe of the lung cannot be identified definitely. It appears to have been drawn into this fibrous mass at the hilum and its identity lost. The right bronchus when opened has no visible connection with the mass above described until serial sections are made through it transversely.

The right pulmonary vein is entirely occluded by a grayish-red thrombus in the hilar portion, the thrombus being about 4 cm. long and 1.5 cm. in diameter.

Left Lung: Weighs 1,300 grams, very large and consolidated. Surface covered with fibrin of varying thickness. On section lower lobe and lower half of upper lobe is of grayish-red, granlar and rather moist as a whole. Bronchi and bronchioles normal caliber. Trachea and primary bronchi show marked congestion of mucosa and coating with thin, frothy fluid. Lymph nodes at hila are moderately enlarged, edematous and congested.

Abdomen: Fibrous adhesions between diaphragm and right lobe of liver.

Kidneys: Numerous cortical abscesses in both kidneys.

Microscopic Examination. Right Lung: Pleura markedly thickened and converted into a dense almost hyaline, connective tissue layer in which are moderate number of blood vessels which show obliterative intimal changes and old thrombosis. Fatty degeneration resembling atheroma in an aorta, with lymphocytes and large mononuclear cells. The underlying lung structure shows rather diffuse interstitial fibrosis. The alveoli are reduced to about one-third the normal size and of these many are partially collapsed, others are emphysematous.

The bronchioles are often collapsed; others are slightly dilated and contain polymorphonuclear leukocytes and red blood cells and desquamated epithelium. There is definite peribronchitis consisting of mononuclear infiltration, and an acute bronchitis with foci of necrosis in the mucosa. Moderate amount of anthracosis. Lining many alveoli which are

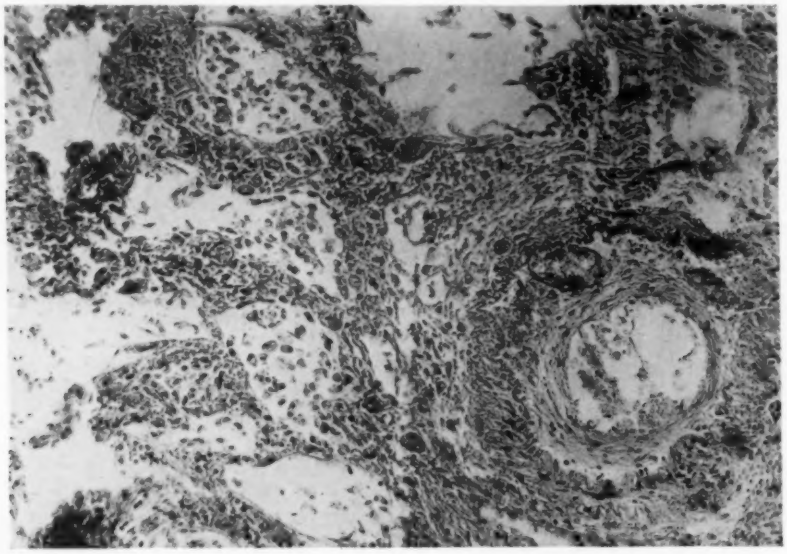

Fig. 13. Within the depths of the right lung marked obliterative vascular changes. The alveolar walls show congestion, thickening and the alveoli contain many desquamated cells and phagocytes containing blood pigment. An acute interstitial pneumonitis also present.

dilated is a hyaline fibrinous material. The blood vessels in the deeper tissues show a marked thickening of the walls, endothelial proliferation and old thrombosis. In some bronchioles the mucosa has disappeared and dilated blood bessels are exposed on the surface, and at these points the lumen contains free blood and desquamated epithelium.

Recent thrombosis of small vessels widespread, and necrosis of vessel walls at points of thrombosis. The large bronchi are narrowed by a thickening of the mucosa which is due to edema, exudation in wall, and also by proliferation and dilatation of capillaries.

Obliterative changes in arterioles and large arteries cover the entire range from acute thrombosis, canalization, to complete obliteration by intimal thickening.

The changes in the larger vessels resemble true arteriosclerosis, but the degree is most unusual to find in a lung. In addition there is rather diffuse acute interstitial pneumonia as shown by polymorphonuclear infiltration in the stroma. There is no evidence of tuberculosis.

The mass attached to the right bronchus is largely necrotic, but shadowy outlines of cells closely packed together can still be discerned. The peripheral portion is still viable, however, and consists of epithelial cells of medullary density, but with a definite adeno-formation as well. Mitoses are not found. It has a dense fibrous capsule, but it is connected with the lumen of the right main bronchus near its bifurcation. It is definitely an adenocarcinoma, with little metaplasia toward a squamous type. No evidence of tumor found within lungs or in any other organ examined.

Left Lung: Shows much thrombosis in the medium-sized vessels, fibrin and leukocytes in smaller vessels and mural thrombi in the larger. There is also diffuse edema and hemorrhage into alveoli. Dilated alveoli are lined by a thick layer of hyalinized fibrin. The pleura, except for a small deposits of fibrin, is of normal thickness. This lung also shows thickening of alveolar walls in many parts. There is partial atelectasis, but no arterial changes like those seen on the right. There is much acute thrombo-angiitis, patchy acute pneumonitis and exudate in the alveoli and bronchioles, polymorphonuclears being abundant, but many of them of immature type.

The lymph nodes from the hila of the lung show anthracosis, chronic and acute lymphadenitis and hyaline changes about some of the arteries. No evidence of active tuberculosis or neoplasm. In a few glands there are old hyalinized tubercles.

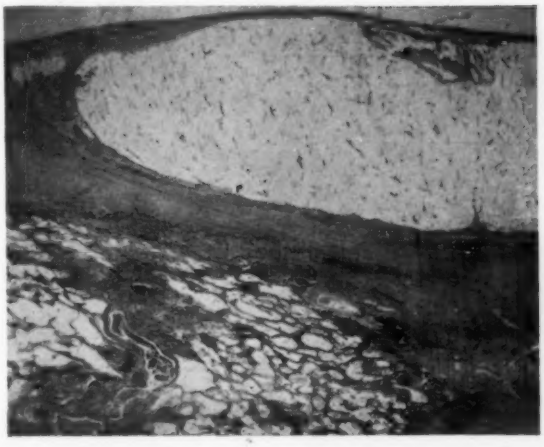

Fig. 14. A low power photomicrograph of the right pleura and underlying lung. The pleura is a dense hyaline layer with large pale yellowish areas filled with fat and lipoid much like an atheromatous aortic plaque. Beneath pleura dense scar tissue, purulent bronchitis, obliterative endarteritis and some air-containing alveoli.

In both lungs there are many bone marrow giant cells in the capillaries and the sections as a whole show evidence of bone marrow exhaustion.

DISCUSSION

The chronology of events in this young man's life viewed in retrospect is most instructive in understanding the significance of various forms of medical evidence. At first following active service in the A. E. F. with a mild exposure to mustard gas, he was invalided by influenza in 1918. Four years later pain developed in his right chest associated with cough. Roentgenograms suggested pulmonary tuberculosis or Hodgkin's disease. On the basis of the latter possibility deep roentgen treatment was begun, in this first course about 2,500 r. In 1924, after a period of relief, coughing returned, with the first hemoptysis. The subsequent nine years showed many periods of remission and seven further courses of deep roentgen therapy, totalling about 15,800 r. While the roentgen evidence during this longer interval was com-

patible with cancer of the right lung, the patient's general condition remained surprisingly good. There was no significant loss of weight and little evidence of anemia. The absence of these usual accompaniments of active malignant growth is worth emphasis.

In 1925 a piece of tissue was removed from the right bronchus, but this was only normal bronchial lining.

Frequent roentgenograms showed slowly progressive fibrosis of the right lung, thickening of the pleura, marked elevation and fixation of the diaphragm, narrowing of the intercostal spaces and retraction of the mediastinal structures to the affected side. It is generally agreed that this syndrome following prolonged deep irradiation is almost pathognomonic of roentgen pleuropulmonitis.

The natural sequelae of this conversion of lung into scar tissue carried with it another complicating tissue factor, i.e. increased vascularity of the bronchial lining. This led to frequent hemoptysis, often of alarming proportions. Irradiation aided in stopping these hemorrhages and was often used for this purpose until 1933.

Thus a vicious circle was established, hemorrhage—deep roentgen irradiation—more scar tissue—increased bronchial vascularity—more deep roentgen treatment—more hemorrhage. All this time while the right lung was almost totally incapacitated for aeration, the left lung had to bear the entire burden and the patient was at the mercy of the first severe infection in his one good lung. Death occurred in 1938, from an acute influenza-like pneumonia—sixteen years after his first symptoms, with secondary septicemia and kidney abscesses.

The necropsy revealed the right lung converted into a structure of fibrous consistence, the size of a man's fist. The pleura was about 4 mm. thick and of almost cartilaginous hardness. Atelectasis was also present wherever there was enough lung structure to permit this to occur. Long search disclosed no evidence of cancer until after fixation serial sections were made. Embedded in a dense mass of fibrous tissue just outside the hilum was an epithelial tumor 2 cm. in diameter with necrotic center and viable periphery. The growth apparently arose from the branch of the right bronchus leading to the upper lobe. The mediastinal lymph nodes contained no tumor.

The diagnosis made at various times of primary lung or bronchial carcinoma was then correct. The treatment was successful from the standpoint of killing most of the tumor and holding the small remnant in a state of subjection. The shadows in the roentgenograms during the last several years were largely those of roentgen reaction in non-tumorous lung tissue. Bronchoscopic drainage was successful for a time shortly before death in relieving symptoms due to blocking of the larger air tubes by mucopurulent exudate and granulation tissue. The hemoptyses of the last year were due to rupture of capillaries in tufts of granulations projecting into the bronchial lumen.

With the gradual loss of volume of the right lung atelectasis doubtless became of constantly increasing importance. The persistent infection within the bronchi and bronchioles with spread to the adjacent parenchyma plus chronic atelectasis with the element of "atrophy of disuse" would explain in part at least the marked obliterative changes within the branches of the right pulmonary artery. Just how much of this vascular damage was due directly to roentgen irradiation is open to conjecture.

The cellular structure of the lung is of a nature that places this organ in the group of less radiosensitive organs. It is a spongy, cavernous tissue, with epithelial and vascular surfaces separated by chambers filled with air, the alveoli. The bronchial epithelium, the cartilage and smooth muscle are more radioresistant than the more specialized cells of parenchymatous organs. Hence it is only natural that high voltage, deeply penetrating roentgen rays have been used very freely when an intrapulmonary neoplasm was attacked. And so

long as the available voltage was in the lower levels little evidence of impaired lung function developed, and likewise little evidence of injury to the tumor.

However, with the high voltages and deep penetrability of modern roentgen equipment, destruction or inhibition of tumors in the chest is being accomplished, at least with a few types. At the same time changes in the non-tumor containing portions of the irradiated lung are being detected. Generally these are of minor clinical import but reports are accumulating with greater frequency which indicate a danger to be appreciated and guarded against. The widespread alteration in lung tissue, of a kind that greatly decreases lung volume, doubles the work of the opposite lung and increases the chances of infection.

Groover, Christie and Merritt[5] in 1922 were apparently the first to call attention to the deleterious effects of roentgen rays when directed upon the lungs. They had used 135 kv. (peak), and a filter of 1.5 mm. of copper. The reaction in the lung was thought due to the greater depth dose resulting from the employment of copper filtration. Several cases were reported of pulmonary "infiltration" following intensive treatment for carcinoma of the breast. They noted an irritative cough at about the time of the skin reaction. The evidence they presented was limited to roentgenograms and clinical course, but they described infiltration in the region of the hilum which spread rapidly and reached its maximum in three to four weeks. Regression then occurred and the appearance of a fibrosis remained. In the early stages a resemblance to influenzal pneumonia was noted. In one of their patients these changes had practically disappeared two years later.

Tyler and Blackman,[11] also in 1922, reported several cases of pleural and pulmonary reactions following heavy roentgen irradiation with various doses, of from 120 to 730 ma-min. before the development of chest symptoms. At first there was pleuritic pain with a non-productive hacking cough. Roentgenograms showed thickened pleura, later bronchial thickening at the hila and infiltration spreading to the lung periphery. There were physical signs of consolidation, dyspnea and cardiac embarrassment. An entire lung was sometimes affected.

Hines, Rose, and others have written on the subject of pleural and pulmonary changes due to roentgen irradiation, but their patients harbored metastatic cancer in the affected lung, and it is not clear how much of the ensuing fibrosis was a pure roentgen effect.

Wintz,[14] in 1923, described a pulmonary infiltration following roentgen therapy, with clinical signs of a central pneumonia and slight cough. This lung shadow disappeared in six to nine months unless intercurrent infection of the lungs developed, the latter giving a bad prognosis. The irradiated lung and pleura were more vulnerable to even mild respiratory infection.

Davis,[2] in 1924, selected 3 cases from the Mayo Clinic as representing true roentgen-ray complications in the lung treated for cancer metastasis. There was an acute onset of symptoms, with non-productive cough, dyspnea, distress and sometimes pain in the affected chest and signs of definite cardiac embarrassment. Early pain, fever, malaise and cough resembled influenzal infection. The patients who were most susceptible to roentgen rays as judged by the skin and systemic reactions showed the most pulmonary involvement. An interval of two or three weeks usually elapsed between the last dose of roentgen radiation and the onset of the first symptoms.

Using dogs and rabbits, Davis studied experimentally the effects of roentgen rays on pleura and lung. He found at autopsy, pleurisy with fluid and adhesions, pericarditis and a reddish-blue discoloration of the lung with non-expansion in these areas which were firmer than normal. The blood vessels showed medial changes. There was peribronchial fibrosis, early alveolar edema and congestion, and epithelial desquamation. Necrosis was noted in the auricular walls.

Desjardins,[3] in 1926, discussed the findings in 20 cases of possible pleuropulmonary changes of roentgen-ray origin, although in some there was carcinoma metastasis to the pleura. He regarded the wave length as unimportant, the chief effect quantitative. The pleura and lung were involved when the dosage approached or passed the limit of normal skin tolerance. Dr. Curtis F. Burnam in discussing this paper said, "It is better to use soft radiation in order to protect the lungs; in the neck and axilla it is more logical to apply as penetrating radiation as possible to produce greater depth effects."

Evans and Leucutia[4] also emphasized the unimportance of wave length in this connection, the changes in the lung being possible when a certain minimum dose of radiation was projected into the tissues by any wave length. However, repeated doses of long wave length were necessary for the summation effects leading to tissue alterations. The tolerance limit for the lungs could not be foretold, but was regarded as probably high. If a dose of 40 to 100 per cent S.U.D. is repeated for the second time, the lung changes become routine manifestations and lead to permanent injury which appear in the early stages as an "infiltration" and later as fibrosis. If a dose of 100–140 per cent S.U.D. was repeated over the lungs for the second time in six months, i.e. before the infiltration had cleared up, the reaction to the second exposure could lead to death. The prognosis following fibrosis was dependent upon the amount of lung tissue involved.

McIntosh[7] was fortunate in being able to study postmortem, changes in the lungs following administration of over 10,000 r to the thorax for inoperable breast cancer. No metastasis was found in the lungs, which were covered with soft, easily broken adhesions. The left lung showed a peculiar consolidation with peribronchial fibrosis. Histologically, there was intense thickening of alveolar walls and some exfoliation of lining cells, peribronchial and perivascular thickening. This was apparently the first postmortem report of the lung pathology of a case of radiation pleuropulmonitis.

Adair,[1] in 1936, studied the effect of preoperative irradiation in primary operable cancer of the breast and compared the effects of roentgen rays and radium. Several cases receiving more than 1,200 r per portal developed cough, dyspnea, pain through the chest, and the dusky color of poor aeration. He noted two types of irradiation pneumonitis as judged by roentgenograms:

1. Segmental or localized area of diffuse thickening radiating outward to the periphery from the mediastinum.

2. More extensive area of thickening of almost the entire lung, heart retracted to the affected side, general fibrosis, and diaphragm elevated.

The author stated that, as the doses increase, more instances of pulmonary change will be manifest. It occurs at all ages, in his series oftener in the younger age groups. Pre-existing bronchitis was not a contributory cause in his opinion. There were no cases with the radium pack until heavier doses were used.

Roentgenologists appear to be far from unanimous in admitting there is such a thing as "radiation pleuropulmonitis" in the proper handling of cases involving irradiation of the lung. Technical errors may account for some reactions, but it is well to emphasize the importance of the Coutard tangential technique to avoid lung damage as much as possible. The experiments of Warren and Whipple[13] in roentgen-ray intoxication showed no lung changes, but their work far from duplicates human exposures since they used too small doses and did not repeat exposures over the same portals. The literature is gradually revealing authentic instances of true radiation effects on pleura and lung, and these will undoubtedly increase as deep roentgen therapy continues to be employed preoperatively or postoperatively for extra-

pulmonary cancer, as well as for non-surgical, primary pulmonary neoplasms, and non-cancerous conditions.

Most writers agree on two main changes within the thorax following heavy irradiation:

1. Pleural, with pain and anatomical thickening.

2. Dense sharply circumscribed roentgen-ray shadows, with bands and linear markings in all directions, retraction of the lung, narrowing of the intercostal spaces, elevation of the diaphragm with fixation, and retraction of the mediastinum to the affected side.

A recent contribution to the scant literature on radiation pleuropulmonitis is that of Nathanson[8] who in 1937 reported 3 cases all of which recovered following roentgen treatment of breast carcinoma. He emphasized that the lesion was essentially benign and that it should not be considered a contraindication to roentgen therapy for suspected cancer within the chest.

In the realm of supervoltage therapy the problem of complicating lung fibrosis is naturally being encountered. The experience of Ruggles[9] with 800 kv. is quoted from his report in 1936.

> We have given up the routine treatment of breast malignancy at high voltage because of the development of severe and disabling fibrosis of the lung coming on three to six months after the cessation of treatment and lasting for months or years. In the early cases we thought we might be dealing with tumor recurrences but the autopsies showed no evidence of carcinoma, only a massive fibrosis. It is accompanied by severe dyspnea and a racking dry cough, both of which last for months.

Experimental studies of radiation effects upon the lungs are few. Wohlauer,[15] in 1909, found congestion two to eleven days after irradiating the lungs of guinea pigs, but no epithelial changes in the alveoli. Tsuzuki,[10] using rabbits, exposed them to 170 kv., 50 per cent of skin dose. He found hyperemia and edema which diminished rapidly. There were also an increase in pigment cells, destruction of peribronchial lymphocytes, and infiltration with pseudo-eosinophils. The work of Davis on rabbits and dogs has already been reviewed as well as the negative findings of Warren and Whipple.

Radium, too, it must be emphasized again, is capable of severely damaging the lung, as Volhard[12] has indicated in his report of a chemist who for many years had prepared and bottled radium preparations without using sufficient care. A few months before death the patient became dyspneic and cyanotic. Autopsy showed almost complete fibrosis of the entire lungs which was believed to be the result of radium damage.

Many of the fundamental cell injuries produced within the chest by irradiation are similar to those seen in abdominal viscera similarly exposed. The changes in the skin and intestines caused by high voltage cathode rays or electrons, as described by Waddell and myself[6] in 1928, working with Coolidge's modification of the Lenard tube, have been seen following roentgen irradiation. The toxic effects of the roentgen rays, radium rays, or cathode rays are probably due to the absorption of disintegration products, the complexity and amounts depending upon the degree of specialization and type of function of the injured tissues.

During the nine years when the case reported in this paper was being given deep roentgen treatments he was in the hands of five or six different roentgenologists. In retrospect it would seem that these consultants were not always in possession of the facts concerning treatments given by the previous radiologist. Each therapist may have considered himself safe in prescribing another course of deep roentgen irradiation. Our present knowledge of the summation of effects in producing roentgen injury to the lung justifies a strong warning to those entrusted with such powerful physical agents. Before giving additional courses of roentgen treatments to a patient

it is practically mandatory that the radiologist be in possession of the facts concerning all previous exposures. To neglect making a reasonable effort to obtain such information may in the future lay the physician open to charges of lack of due care.

SUMMARY

A case is reported of extrapulmonary bronchial carcinoma in a patient treated by deep roentgen irradiation over a period of nine years, receiving a total of about 18,300 r. The tumor, proved only at necropsy, was almost entirely destroyed and a small remnant apparently held in check by this form of treatment. However, a productive pleurisy ensued which was followed by much atelectasis, chronic interstitial fibrosing pneumonitis, and chronic bronchitis with hemoptyses from intrabronchial granulations. A marked degree of obliterative change occurred throughout the arterial tree of the affected lung. Death resulted from bronchopneumonia in the opposite lung due to *Staphylococcus aureus*, with renal abscesses and septicemia.

The value of radiotherapy in the treatment of cancer of the lung is emphasized, but the pleural and pulmonary damage which may follow such measures should be appreciated and guarded against as much as possible. An increase in such complications is prophesied unless improvements in radiation technique are forthcoming.

The survival time following demonstration of bronchial carcinoma either by roentgen rays or biopsy is usually short, but this case demonstrates that radiotherapy may prolong life very materially, provided metastasis has not occurred. The sixteen year interval between the original diagnosis and death is possibly the longest yet recorded for this type of neoplasm treated by non-surgical methods.

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DISCUSSION

DR. JOHN R. CARTY, New York City. Dr. Jacobsen's detailed report is timely and of great interest. Anyone who has had sufficient experience in this field and has carefully studied his cases roentgenographically as well as pathologically, wherever possible, will have to admit that radiation fibrosis is a definite complication of radiation therapy to the chest in large carcinolytic doses. I have had the opportunity of studying 5 cases of radiation fibrosis which were produced during the course of therapy for

carcinoma of the breast. These cases are particularly interesting because as far as we could determine they were free from extraneous factors introduced by the presence of carcinoma in the pleura or lung fields. In all 5 cases the first thing which we noticed was a tenting of the diaphragm. This occurred even though the upper half of the chest was treated. This was followed by a clouding directly over the treated area. Subsequently the mediastinal contents were displaced to the affected side, and the diaphragm elevated. Outside of a slight inconsequential temporary dry cough, 2 of these patients had no symptoms whatever. Three patients had severe and very annoying cough. Two of these 3 patients had repeated attacks of pneumonia, but in none of these did atelectasis, abscess formation or bronchiectasis develop. In none of these patients was there any significant previous history of pulmonary infection.

It is my impression that the presence or absence of pre-existing infection in the lungs has a great deal to do with the seriousness of radiation fibrotic changes. All of us have seen instances in non-treated cases where atelectasis persisted only to clear after a considerable period of time without leaving a residual process. On the other hand, in other instances an atelectasis lasting only for a short while may be followed by serious pulmonary infection and in the latter type of case one often gets a history indicating previous chronic pulmonary infection. When we attempt to kill carcinoma cells it becomes necessary to deliver a very heavy dose to the tumor. Our problem, therefore, is to reduce the damage to normal tissue as much as possible. I do not feel that a local fibrosis immediately around a tumor is undesirable. On the contrary, I believe that it may actually aid in holding the cancer cells in check. However, if this fibrosis is spread over a very wide area to include much normal lung, trouble is very apt to ensue. This is particularly true because of the fact that so many bronchogenic carcinomas are already associated with serious pulmonary infection as a complication. This becomes more apparent when we consider that there is so often a blockage of the bronchus and the debris caused by an activation of the inflammatory process by the irradiation cannot find an exit. At present we are going over the cases of bronchogenic carcinoma which we have treated and one receives a distinct impression that roentgen therapy may be contraindicated in some cases where there is atelectasis plus definite evidence of infection.

In order to deliver the radiation in the most efficient manner, multiple portals of entry for the radiation should be used. It is very convenient to have roentgenograms of the chest in the posteroanterior and lateral positions for planning the portals. If the tumor is not too extensive, a large dose can be administered with a minimum of damage to normal structures.

There is another type of injury which Dr. Jacobsen has not discussed, that is pathological fractures caused by excessive irradiation over a local area of the rib. These are extremely difficult to differentiate from a metastatic lesion and often time alone can differentiate. The bone is eburnated and eventually fractures, with little or no attempt at healing. At first the fracture may be painful but this sometimes wears off and a false joint may form.

I wish to emphasize that radiation fibrosis is usually produced only by prolonged treatments with heavy doses. I have never seen pulmonary fibrosis following therapy of the chest with the dosages used for the treatment of inflammatory conditions. These undesirable sequelae should not deter us from using roentgen therapy when indicated, but should serve to impress us with the necessity for skill and experience and adequate apparatus for this type of work.

THE EFFECTS OF RADIOTHERAPY AS RECORDED BY SERIAL COLOR PHOTOGRAPHY*

By LLOYD A. CAMPBELL, M.D.
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SERIAL color photography of selected cases gives the radiologist a more accurate means of recording the effects of radiotherapy. The prime requirement in clinical photography is that the lesion be reproduced with practically microscopic detail to give an accurate delineation of the area of interest to definitely show its pathologic nature. To this, color adds a realism so valuable to scientific records.

Serial color photography is particularly advantageous in demonstrations to large groups, as the teaching of students, or it may lend itself to the instruction of the individual practitioner in the case of some specific tumor. Often one wishes to demonstrate to the patient the course of a similar case, and with color photographs the radiologist can produce visual evidence to assure the apprehensive patient: an essential to satisfactory treatment and the cooperation of the patient.

On many occasions the radiologist would like to preserve and study certain tissue reactions that occur in such rapid succession following some therapeutic technique, instead of merely observing the change in his routine examination. The beginning erythema, mucositis, the extent of the sloughing area, and any degree of skin reaction can be accurately and permanently recorded in color as they appear. This can be done with little change in the general office procedure.

In all serial photography one should inconvenience the patient as little as possible, for any manipulation that is painful or tiresome to the patient is a handicap to succeeding exposures. It is with this in view that one must arrange his camera and lights so that they become a part of the examination, and the patient is not alarmed by unusual preparations.

In order that a comparison with other exposures may be valuable the factors of distance from lens to subject, time, diaphragm stop, and lighting should not be varied, and an established photographic technique should be followed with these factors remaining as constant as each case will allow. This can be determined with some experimentation upon the part of the operator, particularly as to the adaptability of his type of apparatus to these requirements.

Accuracy of exposure is far more important in color than in monochrome photography. An underexposure will result in a muddy, dull transparency with a predominance of blues and purple, while an overexposure will give a thin, washed-out positive transparency with a predominance of yellow and reds. To give an accurate exposure one should depend upon his light meter for the correct settings, varying this slightly to allow for the amount and color of reflected light from the subject and surroundings to be photographed.

Color photography as an office routine is divided into two distinct fields—surface and cavity exposures. As the best color film is available in the 35 mm. rolls containing eighteen exposures, the miniature camera not only contributes to economy but lends itself to rapid, easy adjustment in both fields of work. In the choice of a camera one should select that type which will allow a short working distance, for detail and color shadings are best expressed by close-ups. We find that most of our surface pictures are taken at an 8 or 12 inch distance, these being fixed focus points for the attachment to the Contax which we use. Color pictures at an 8 inch distance give one-fourth the size of the original image and in certain small lesions where one desires

* Read at the Twenty-fourth Annual Meeting, American Radium Society, St. Louis, Mo., May 15–16, 1939.

an image of natural size, the apparatus for cervical photography is used.

The general problem of focus is most important and demands careful attention. It is easily accomplished while viewing the patient and field of exposure by merely moving the camera to or from the subject to converge the images, such as a small spot or highlight near the center of the field. This allows one to quickly compensate for the unavoidable movement of the patient. Some[4] use a "distance-measuring stick" to determine the correct focus, which would seem to provide a greater source of error than the direct observation of the patient.

Fig. 1. Camera with fixed-focus attachment and sliding device for rapid surface photography.

The time spent in serial color photography can be minimized by the use of a proper stand to mount the camera. We find that a single rod, adjustable for height, allows one to get closer to the table in cervix cases and affords less inconvenience to the patient in surface photography. This is set in an extra heavy base to provide stability,

Fig. 2. Camera arrangement for photography of the cervix showing the heavy stand mounted on ball casters.

Fig. 3. Camera arrangement for photography of the cervix with mirror-reflex focusing device, telephoto lens, and tilting head.

Fig. 4. Black nickel speculum for photography of the cervix with the lights mounted to the upper blade.

for accidents on the part of the operator or patient do sometimes occur, with disastrous results. The stand is mounted on ball casters upon which it is easily moved or positioned. Fastened to the rod is a standard aluminum ball and socket joint upon which a device for fine adjustment is located. This allows the camera to be moved to or from the subject in the selected line of vision a distance of $3\frac{1}{2}$ inches, and thus obviates the movements of the entire stand when one is working at a fixed focus.

In photographing the usual case we find that two R_2 photofloods will provide economical, uniform, and satisfactory lighting. One is mounted on a flexible stand while the other is a hand reflector that can be held in the various positions to distribute the light to special locations. This is particularly useful in photographing lesions of the mouth where adequate lighting is more difficult. In most surface work each light is accurately placed at a distance of 15 inches from the patient in order that the intensity remain a constant.

In cavity photography we include the deeper lesions of the mouth, the pharynx, and particularly those of the cervix. In each of these locations good color transparencies depend to a great extent upon the proper illumination. Other operators[1,2,3] have ex-

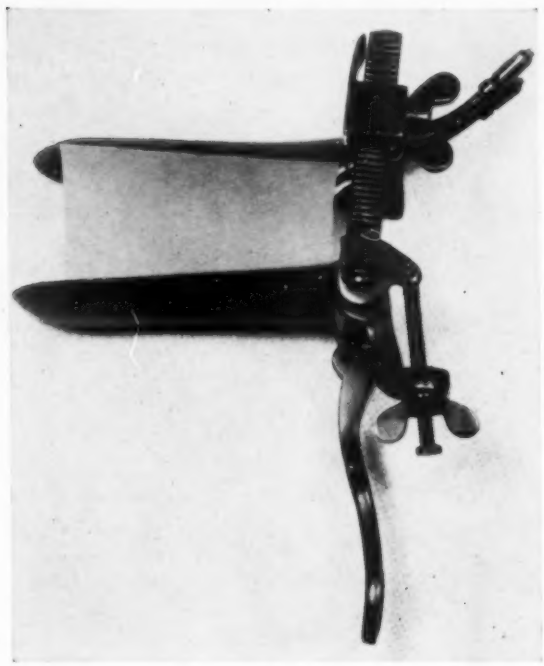

Fig. 5. Speculum with Penrose drain over blades to prevent vaginal walls and pubic hair from entering the field of vision.

Fig. 6. *A*, squamous cell carcinoma of the cervix, Grade 2, patient aged twenty-three, showing involvement of the entire right portion by a hard indurated mass of a glazed or bluish-white color. Photograph taken in operating room. *B*, case *A* five months after treatment. *C*, squamous cell carcinoma of the cervix, Grade 2, patient aged twenty-nine, involving the entire cervix. *D*, case *C* five months after treatment. *E*, squamous cell carcinoma of the cervix, Grade 4, showing extensive ulceration with areas of infection. Patient, aged fifty-five. *F*, early squamous cell carcinoma of the cervix, Type 1, Grade 2, five years after treatment. Patient, aged twenty-six. *G*, ulcerative carcinoma of the cervix, Grade 3, showing extensive necrosis and beginning excavation. Patient, aged forty-one. *H*, squamous cell carcinoma of the cervix showing extensive cavernous excavation of the vaginal vault following destruction of entire cervix by the ulcerative process. Patient, aged fifty.

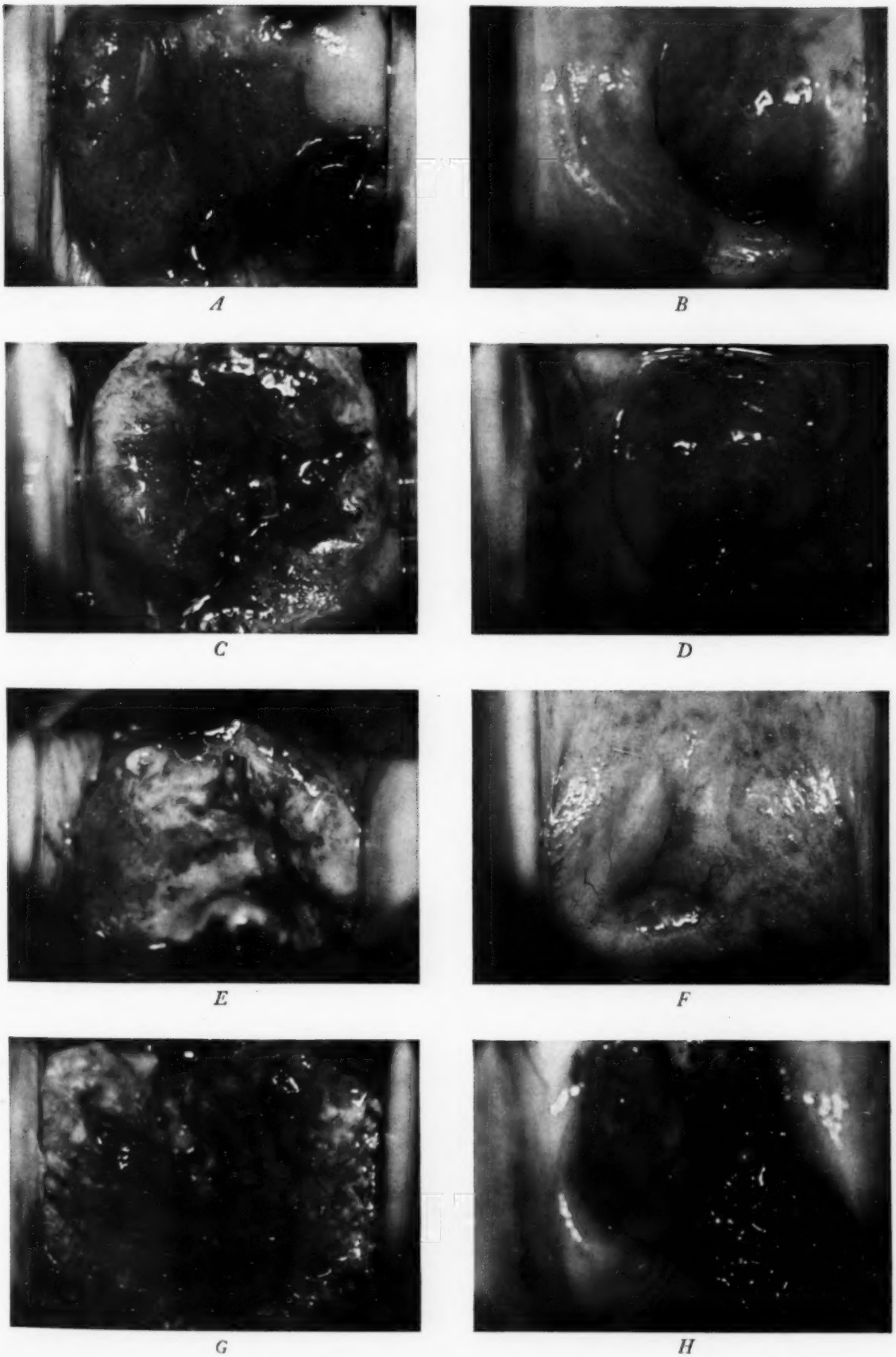

FIG. 6 (See explanation on facing page)

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perienced this difficulty, and each has devised their lights and specula to overcome it. In photography of the cervix we use our ordinary examining speculum, the design of which permits the largest variable opening while the blades are short enough to permit the cervix to come forward in those cases where it is not fixed. Attached to the upper blade are two 4.5 volt wide focus lights with the carriers so arranged that the cervix remains in the path of illumination regardless of the position of the upper blade. These lights are of sufficient brightness so that they approach, as closely as possible, that of a photoflood to which the kodachrome film is adjusted. The resulting transparencies will have truer color values than those taken with a light of lower intensity where the red of the filament predominates. The speculum is plated with black nickel to prevent reflections. A large size Penrose drain is placed over the blades as Galloway[3] recommends. This holds the lateral vaginal walls perpendicular and also prevents the encroachment of the pubic hair upon the field of vision. The time factor can be lengthened, for movement of the cervix seldom occurs, and one can use a much smaller stop, resulting in a greater depth of focus.

In order that the detail of cervical lesions be reproduced in natural size and also to allow a satisfactory working distance, a telephoto lens is required. We use an 85 mm. F_4 lens attached to a reflex-mirror focusing device which affords a direct view of the area to be photographed. When the camera is focused, pressure on a single cable release lifts the mirror and opens the camera.

In the routine examination of malignant lesions of the cervix before or after radiotherapy, we use the same technique as when photography is contemplated. The actual taking of the picture requires only that the stand be moved into position and the camera focused, for the factors of distance, light, stop, and time have all been determined. The resulting color photograph is less liable to error and affords sufficient accuracy to give a comparison with others taken in like manner.

The exchange of lens and focusing device as required when shifting from cavity to surface areas or vice versa is readily accomplished and should always be done before the preparation of the patient.

After processing, the transparencies are catalogued and filed for ready reference. A slide viewer permits the study or demonstrations of these photographs at a desk, or they can be projected in any standard lantern.

SUMMARY

Serial color photography as an office routine gives the radiologist an accurate record of the effects of radiotherapy. An apparatus for surface and cavity photography is described.*

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* For discussion see page 263.

TREATMENT OF LARGE PROTUDING CARCINOMAS OF THE SKIN AND LIP BY IRRADIATION AND SURGERY*

By HOWARD B. HUNT, M.A., M.D.
OMAHA, NEBRASKA

THE large, protruding, bulky carcinoma of the skin or lip presents a discouraging and formidable appearance, but experience shows that this type of tumor responds well to adequate treatment by irradiation or surgery. Ewing[2] and others have called attention to the favorable prognosis in papillary carcinoma of the lip and skin, pointing out that the tumor may grow to large size with no metastases to regional lymph nodes. Hofmann[5] has correlated gross morphology of carcinoma of the cervix uteri with curability. He finds the index of five year clinical cures in Stage II lesions is 54.7 per cent with everting growths and 37.5 per cent with inverting growths. This statistical study justifies a better prognosis for the bulky protruding tumor than for the ulcerating invading lesion.

Diverse opinions have been held regarding the best method for treatment of bulky carcinomas. New and Figi,[8] and others, have advocated surgical resection of the bulky tumor and adjacent tissue with immediate repair. Radiotherapy was held by them to be incompetent on the premise that surgery would subsequently be necessary to repair the post-irradiation deformity. Quick[9] and his associates have advocated electrosurgical resection of the protruding portion of the bulky oral carcinoma to allow direct implantation of radon seeds in the base for control of the lesion. Ablation of cauliflower growths of the cervix uteri by electrosurgery prior to application of radium is practiced by many radiotherapists for facilitation and speeding of placement of applicators. Bowing and Fricke[1] prefer to treat bulky carcinoma of the cervix entirely by serial applications of radium to the shrinking mass, while Healy[4] and many others produce preliminary regression by roentgen rays prior to application of radium. Widmann[12] advocates treatment of large thick carcinomas of the skin by unfiltered roentgen rays generated by 127 kv. Therapeutic dosage is then calculated at the base of the tumor, with addition of sufficient surface dosage to offset radiation absorbed while traversing the tumor. C. L. Martin[6] has advocated similar treatment for bulky carcinomas of skin and lip by intermediate roentgen therapy with the addition of low content platinum filtered radium needles through the base of the tumor. Gratifying results are shown by all writers, indicating that the best method may be that with which the therapist is most familiar.

The following cases are being presented to fortify the courage of the therapist who is presented by a patient with a large bulky carcinoma of skin or lip. It is important that the doctor approach these cases with justified hope and courage because patient and friends are often unduly disheartened by gross disfigurement from the lesion. Furthermore, we wish to call attention to the relative lack of deformity which is finally evident after eradication of the neoplasm by irradiation. In the majority of cases, we expected to effect a plastic repair but found the spontaneous restoration of contour and function to be surprisingly satisfactory rendering operative repair unnecessary.

CASE REPORTS

The following case presents a protruding basal cell carcinoma of the forehead successfully treated by surgical resection and

* From the Tumor Clinic, University of Nebraska Hospital. Read at the Twenty-fourth Annual Meeting, American Radium Society, St. Louis, Mo., May 15–16, 1939.

Fig. 1. Case 1. *A*, large polypoid basal cell carcinoma on forehead resected surgically on July 13, 1936. *B*, defect was closed by a thick split-graft from the thigh; no recurrence to date.

restoration of skin by a thick split-graft. The lack of infiltration adapted this lesion very well to such management. We believe that the lesion could have been controlled by radiotherapy.

Case 1 (Univ. Nebr. Hosp. No. 54069). Mrs. I. H., housewife, aged fifty-three, entered the hospital on July 7, 1936, presenting the clinical picture of pellagra and a large tumor on the forehead. The tumor had developed over a period of seven years to a rounded nodular mass 4.5 cm. in size (Fig. 1). It was removed by Dr. Charles McLaughlin and a thick split-graft from the thigh applied twelve days later. Microscopic section showed a degenerating basal cell carcinoma with occasional areas of keratinization. There has been no recurrence and a good cosmetic result was obtained. Symptoms of pellagra were relieved by a high vitamin diet.

Carcinoma of the scalp as illustrated by the following case is well adapted for radiotherapy. Local epilation simplifies cleansing of the wound. Plastic repair in this region is not particularly gratifying. The lesion can be controlled by irradiation providing the blood supply is fairly good. A question might be raised with regard to what possible relation there was, if any, between the terminal cerebrovascular disease and the rather penetrating local irradiation.

Case 11 (Univ. Nebr. Hosp. No. 54554). Mrs. M. M., housewife, aged seventy-two, entered the hospital on September 14, 1936. A pea-sized nodule noted on the left occipitoparietal region ten years previously had slowly become a fungating ulcerating mass 1.5 cm. thick and 6 cm. in diameter which was firmly fixed to the scalp (Fig. 2). Biopsy was reported by Dr. J. P. Tollman as a keratinizing basal cell carcinoma (Fig. 2*C*).

Four roentgen treatments of 575 r (measured in air) each, 200 kv. (peak), no filter, 20 cm. distance, were given from September 14 to 23, 1936, and 2,150 mg-hr. of interstitial radium, in 16 needles of 0.5 mm. platinum wall were delivered from September 14 to 19, 1936. The tumor regressed promptly and the skin was fully healed after five months. She died fifteen months following treatment apparently from cerebrovascular disease. No recurrence of cancer became evident.

The unusually large polypoid, adenogenous carcinoma presented by the next case was readily treated by interstitial radium in its base following electrosurgical ablation of the pendulous portion of the tumor.

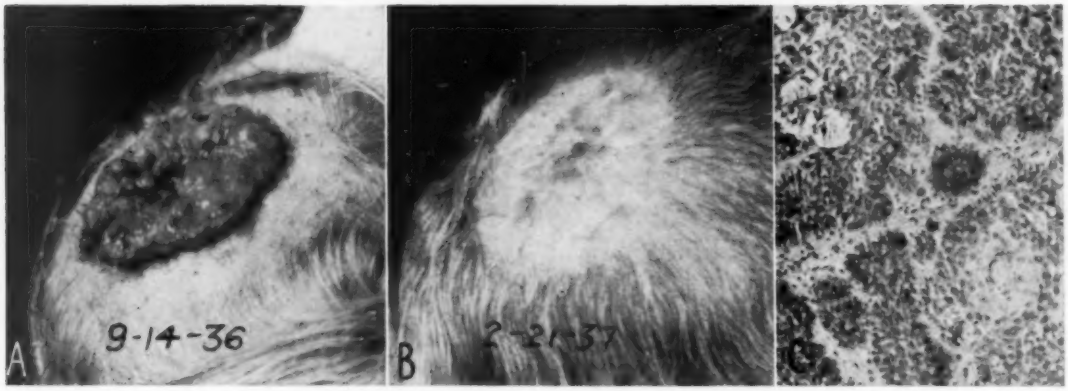

Fig. 2. Case II. *A*, broad basal cell carcinoma of the scalp treated by roentgen rays and interstitial radium. *B*, disappearance of tumor and healing of skin. Died fifteen months later of cerebrovascular disease. *C*, photomicrograph shows clumps of uniform cells, some central keratinization and a moderately vascular stroma—adenoid epithelioma.

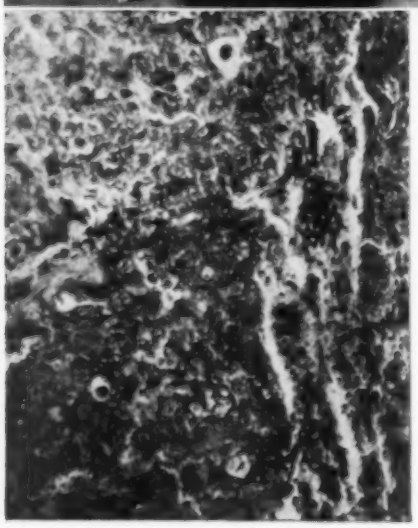

Fig. 3. Case III. *A*, protruding carcinoma involving lids and cheek treated by radium implantation in base after electrosurgical ablation of pendulous portion. *B*, appearance nearly four years later, showing good preservation of tissues but with some retraction of the lids. *C*, adenogenous type of basal cell lesion, in general poorly differentiated but with some keratinization and pseudo gland formation.

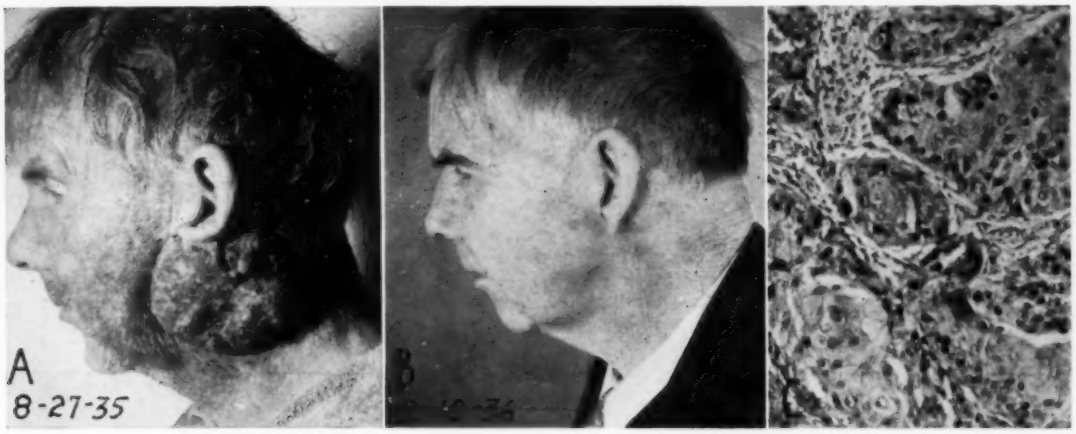

Fig. 4. Case iv. *A*, bulky carcinoma treated entirely by roentgen and radium irradiation. *B*, three months later—no evidence of carcinoma, minimal scarring. *C*, Grade 2 squamous cell carcinoma with much keratinization and abundant vascular stroma.

Case iii (Univ. Nebr. Hosp. No. 54191). F. M., male, farmer, aged sixty-five, entered the hospital on August 13, 1935. A warty growth began in the left infra-orbital region two years before entry and rapidly increased in size. An orange-sized, polypoid, friable mass about 6 cm. in diameter obscured the left eye with invasion of the entire left lower lid and lateral border of the upper lid (Fig. 3). No lymphadenopathy was evident. Biopsy was reported by Dr. J. P. Tollman as showing an adenogenous type of basal cell carcinoma, in general poorly differentiated but showing areas of keratinization and pseudo gland formation (Fig. 3*C*).

The pendulous portion of the tumor was removed with the endotherm knife. Copious oozing hemorrhage was controlled better by compression than by electrocoagulation. Interstitial radium was administered by thirteen needles through 0.5 mm. of platinum to the basal area of the tumor 4×4×6 cm. for 1,980 mg-hr. A further application of 1,200 mg-hr. was administered to questionable residual areas of induration two months later. The area showed complete healing after five months and there has been no recurrence of cancer after nearly four years. The lower lid is short, smooth and lacking in eyelashes. A plastic elevation of the lower lid is being considered. Early cataracts are present in both eyes, more advanced in the left lens probably due to combined senile and post-irradiation changes.

In the following case, we chose to treat a large bulky tumor similar to the last one entirely by irradiation with an equally satisfactory result.

Case iv (Univ. Nebr. Hosp. No. 51075). J. G., male, stonecutter, aged seventy-two, entered the hospital on August 27, 1935. A warty growth had gradually developed in the scar of an old rat bite below the left ear during the ten to fifteen months prior to entry. A rounded, sessile, friable, infected tumor about 5 cm. in diameter projected from the left side of the neck beneath the ear (Fig. 4). Biopsy according to Dr. Tollman revealed a Grade 2 squamous cell carcinoma with much intercellular stroma (Fig. 4*C*).

From August 28 to September 5, 1935, 2,800 r of 130 kv. (peak) roentgen rays, filtered through 0.25 mm. aluminum was delivered to the tumor and marginal zone. Interstitial radium was delivered through the base of the tumor by fifteen needles, filter 0.5 mm. of platinum, for a total dosage of 2,665 mg-hr. from September 6 to 12, 1935.

He returned six weeks later with nearly complete disappearance of the lesion except for a persistent, indurated rim. An additional dose of 2,000 mg-hr. of radium was delivered along the the border from the surface through 1 mm. platinum at 5 mm. distance. The skin was fully healed after three months and he remains well after nearly four years.

The following case shows the adequacy of application of radium on the surface for control of a relatively large, flat squamous

cell carcinoma below the eye. Roentgen therapy energized by low or intermediate voltage, with a lead shield over the eye, would have been preferable in view of a cataract now beginning in the eye after five years.

Case v (Univ. Nebr. Disp. No.63513). H.B., unemployed laborer, aged sixty-eight, entered the hospital on July 20, 1934, presenting a sessile, everted, ulcerated tumor about 2×4×5 cm. in the left infra-orbital region of six months' development (Fig. 5). An adjacent plaque had been present beneath the bridge of his glasses for many years. Biopsy was reported as Grade 2 squamous cell carcinoma by Dr. J. P. Tollman. A small mass removed from the submaxillary region showed carcinoma invading the salivary gland, probably metastatic. The primary lesion on the cheek was treated by 80 mg. of radium embedded in wax, filtered through 1 mm. platinum distributed in ten foci over an area 4×5×4×6 cm. delivered from 1 cm. distance for a total of sixty-eight hours at daily intervals from July 25, 1934 to August 3, 1935, 5,440 mg-hr. An effort was made to shield the left eye by 1 cm. of lead. The tumor receded rapidly and the skin was healed after three months. After five years he shows an early cataract in the left eye but can still read coarse newspaper print with it. A small carcinoma has recently appeared on the upper lid and is being irradiated at this time.

Two patients with large papillary carcinomas of the lower lip were successfully treated by a combination of roentgen rays with subsequent interstitial radium. In each case a subsequent plastic repair was originally planned but later proved to be unnecessary.

Fig. 5. Case v. *A*, sessile squamous cell lesion treated by radium in wax mold. *B*, three months later—no evidence of cancer, essentially no deformity.

Case vi (Univ. Nebr. Hosp. No. 56276). P. K., male, carpenter, aged sixty-eight, entered the hospital on February 26, 1937. He noted a "fever blister" on lower lip two years previously which had developed into a large tumor covering the lower lip. The entire lower lip was replaced by a fungating ulcerating mass extending from angle to angle and down to the chin (Fig. 6). Submaxillary lymph nodes were palpable bilaterally. Biopsy revealed a Grade 2 squamous cell carcinoma. Treatment consisted of 2,000 r of 200 kv. (peak) radiation filtered through 0.5 mm. Cu to right and left submaxillary regions and to the lip in ten days cross-

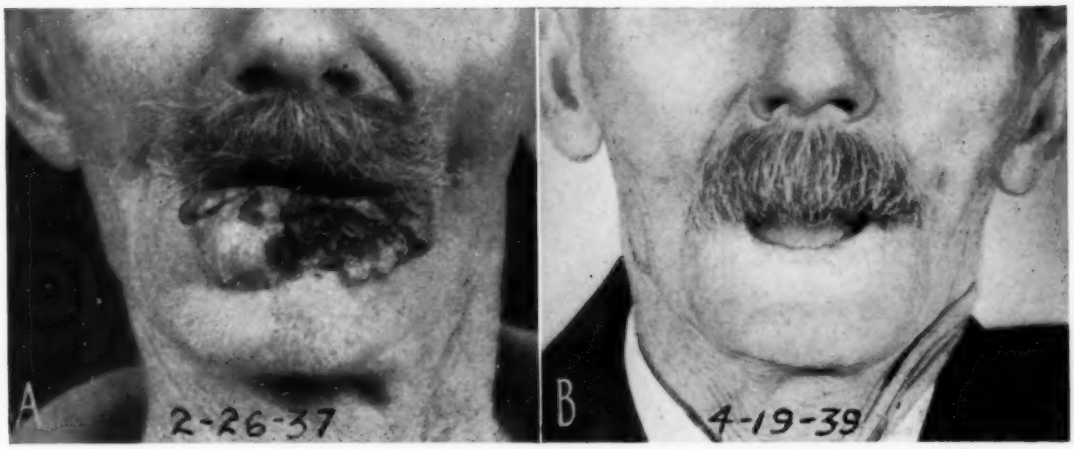

Fig. 6. Case vi. *A*, necrotic papillary carcinoma of the lip treated by roentgen irradiation followed by interstitial radium. *B*, lip shows little deformity and good function with no evidence of carcinoma.

firing the chin. This was followed by 1,200 mg-hr. of interstitial radium in six days, placed in a palisade through the lower lip. The lesion gradually regressed leaving a short, somewhat irregular but well functioning lower lip. The submaxillary nodes slowly regressed and have shown no recurrent enlargement at repeated examination. He is well after two years.

The following case shows a dramatic regression of an enormous carcinoma of the lower lip occurring after relatively small doses of roentgen radiation and interstitial radium.

Case vii (Univ. Nebr. Hosp. No. 56944). G. S., male, retired farmer, aged eighty, entered the hospital on May 5, 1937. A small lump, noted on the lower lip nine months previously, had grown rapidly to enormous size. A soft, friable, fungating mass 4×5×10 cm. covered the entire lower lip and obscured the mouth (Fig. 7). Submaxillary nodes were slightly enlarged. Biopsy showed Grade 3 squamous cell carcinoma.

The superficial half of the tumor was cut away with scissors and bleeding controlled by compression. From May 6 to 24, 1937, 2,500 r was delivered to the right and left submaxillary nodes and to the lower lip and chin. At his return one month later, a narrow rim of induration persisted along the border of the lip. Radium was applied interstitially along this rim by low content 0.5 mm. platinum needles for 800 mg-hr. The neoplasm disappeared completely. The lip was well formed and no plastic repair was desirable. The lymph nodes regressed. He died suddenly on December 12, 1938, from a "heart attack." No recurrence had appeared during this interval.

The following case shows a very exten-

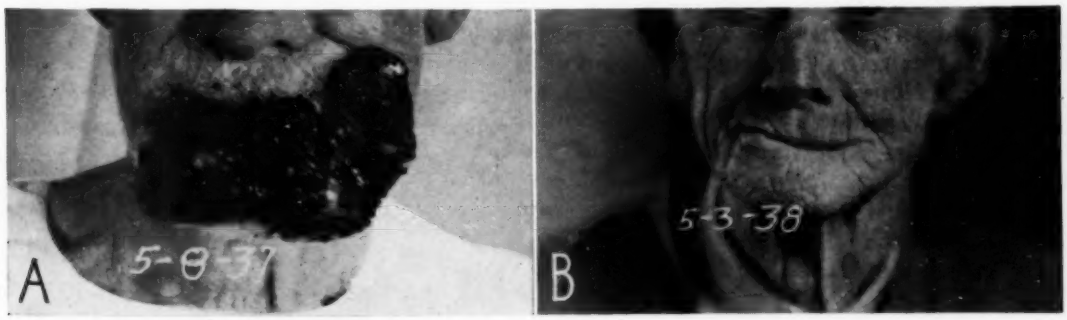

Fig. 7. Case vii. *A*, enormous carcinoma of the lower lip treated by roentgen irradiation followed by interstitial radium. *B*, complete regression of tumor with very little subsequent deformity of lip.

sive highly malignant carcinoma of the lip, recurrent after inadequate roentgen therapy, successfully controlled by surface and interstitial radium therapy.

Case VIII (Univ. Nebr. Hosp. No. 5055). J. P., laborer, aged sixty-five, entered the hospital on March 30, 1935, complaining of a recurrent cancer of the lip. A papule on the lower lip noted four years previously had been treated by endothermic removal and one dose of roentgen rays, about 1,000 r, three years before. Initial regression had been followed by a recurrence with rapid growth for three months. The lower lip was replaced by an ulcerating nodular mass 2×3×6 cm. in size (Fig. 8). Biopsy showed a Grade 3 to 4 squamous cell carcinoma (Fig. 8*C*). Lymph nodes were palpable in submental and submaxillary regions.

Treatment consisted of 2,500 r (measured in air), 0.23 Å effective wave length, delivered to the right and left submaxillary regions. The lower lip was treated by 1,700 mg-hr. of radium in a wax mold filtered through 1 mm. of platinum during seven days and 1,900 mg-hr. of interstitial radium three weeks later with the above noted roentgen therapy administered in the interim. A further treatment with 1,100 mg-hr. of interstitial radium was given two months later due to some residual induration.

The cancer disappeared, enlarged nodes regressed and plastic repair of the lower lip was unnecessary due to excellent restoration. He remains well with no apparent recurrence after four years.

Fig. 8. Case VIII. *A*, recurrent, highly malignant carcinoma of entire lower lip treated by radium from the surface and interstitially. *B*, four years later—no evidence of cancer, only slight irregularity of lower lip. *C*, Grade 3 to 4 squamous cell carcinoma showing numerous mitotic figures, anaplasia and massive infiltration with moderate vascularity.

PATHOLOGY

The histological appearance of bulky carcinomas allows classification into the usual squamous cell carcinomas and aberrant basal cell carcinomas with keratinization. The latter group of tumors has been called "simple adenoid epithelioma" by Ewing.[2,3] He describes the lesions as follows:

At the usual seats of rodent ulcer, larger and usually more active tumors often arise in which there are large alveoli lined or filled with cylindrical or cuboidal epithelial cells of a type intermediate between squamous epithelium and the duct cells of dermal glands. These tumors are not cystic, they are usually sharply circumscribed and relatively large, and their course is progressive with occasional involvement of lymph nodes or ulceration.

These tumors show the alveolar arrangement of basal cell carcinomas and the tendency toward keratinization of squamous cell carcinoma as shown in Figures 2*C* and 3*C*. Varying grades in activity of growth and extent of keratinization do occur in this group of tumors. Squamous cell carcinomas vary in appearance according to the amount of connective tissue stroma, massing of cells and degree of differentiation. In general, the squamous cell carcinomas show an intermediate grade of mitotic

activity and anaplasia, as in Figure 4*C*. Occasionally, a very highly malignant tumor may be encountered, as in Figure 8*C*. The majority of bulky tumors in this series were superimposed upon an indolent lesion of some years' duration in which growth was suddenly accelerated. The surprising lack of metastases even with a highly anaplastic, extensive tumor as in Case VIII appears to be quite characteristic of the protruding carcinoma. Only 1 of the 8 cases showed evidence of metastasis and that was controlled by simple excision.

RADIOSENSITIVITY

The remarkable radiosensitivity of these papillary growths, as shown particularly by Cases VI and VII, has been noted by Ewing[3] and others. He attributes the response to the vulnerability of the delicate vessels abundantly distributed through the tumor. Disappearance of the tumor depends in part on necrosis and liquefaction (Fig. 3*C*) due to infarction. The radiosensitive tumor is usually soft, pinkish, and granular in appearance. Stewart[10] points out that hard, warty squamous cell carcinomas with well developed vessels are usually more resistant to irradiation. Stout,[11] in analyzing a small group of oral carcinomas, reported that papillary character had little bearing on radiosensitivity. This might have resulted from the presence of low grade papillomas in his series. Benign papillomas, adenoma malignum and such indolent low grade tumors are not radiosensitive. Radiosensitivity is said by Stewart to depend on the embryonal quality of a tumor, the degree of anaplasia, the fundamental tissue of origin, the degree of papillary character, the circulatory status of the tumor, the nature of the tumor bed, the presence or absence of infection and the general health of the patient.

TREATMENT

The morphological characteristics of the protruding tumor facilitate treatment. In general, the tumor has grown out away from the healthy tissues with little invasion of the tumor bed. Eradication of the neoplasm can therefore be accomplished with relatively little attending loss of normal tissue and surprisingly little subsequent deformity.

Surgical resection is adequate for eradication of the bulky, protruding carcinoma. The defect can be closed by a skin graft, sliding flaps or other reparative procedures.[8] Repair by the thick split-graft, as shown in Case I, speeds healing and gives a good cosmetic result. The subsequent deformity is usually greater after surgery than following irradiation due to the necessary sacrifice of surrounding healthy tissues. Surgical resection of a large papillary tumor of the lip by the average surgeon causes much more disfigurement and disturbance of function than irradiation. On the other hand, the deforming, invasive, ulcerating carcinoma of the lip is better treated by surgery than by irradiation in case it is still resectable. The benign or low grade papillary tumor is better treated by surgery than by irradiation due to the radioresistance of the lesion. In general, we believe irradiation is definitely superior to surgical resection in the treatment of bulky, actively growing carcinomas of skin and lip.

Surgical removal of the protruding portion of a polypoid carcinoma facilitates direct irradiation of the base as in Cases III and VII. Radium can then be applied on the surface or interstitially and roentgen rays can be applied in the conventional manner or by the method of Chaoul. Resection of the bulk of the tumor removes infected tissue and reduces the amount of destroyed tissue which the patient must absorb and eliminate through his body. Hemorrhage is copious at the time of resection due to the vascularity of the lesions, and is more readily controlled by compression than by electrocoagulation, in our experience.

Radiotherapy alone is adequate for the control of bulky carcinoma of the skin and lip as in Cases II, IV, V, VI and VIII. The total dosage administered to each carcinoma in this series was about 5 to 10 erythema doses during a period of three to five weeks. Either roentgen rays, radium, or

a combination of the two, can be used. External irradiation alone seems most valuable in the flat tumors or in badly infected lesions. Roentgen rays should be so administered as to avoid overpenetration with resulting devascularization of the healthy zone below the tumor. It is desirable to use a short distance, 25 cm. or less. The kilovoltage should be between 85 and 130. We have observed avascular post-irradiation ulcers from the administration of 5×900 r (measured in air) to areas 1.5 cm. in size when using 200 kv. radiation but not when using 100 kv. unfiltered or lightly filtered radiation in this dosage. It should be remembered that most oil-immersed, water-cooled deep therapy tubes have an equivalent filtration of 0.15 to 0.25 mm. of copper.

Roentgen rays combined with interstitial radium (or radon seeds) as used in Cases II, IV, VI and VII provide a potent well distributed irradiation. The preliminary use of roentgen rays will shrink the more radiosensitive portions of the tumor, making more evident those areas in which additional dosage is indicated. Interstitial irradiation provides great flexibility in localization of dosage. Extensive infection of the tumor and surrounding tissues contraindicates interstitial placement due to spread of infection and poor tolerance of infected tissues for radiation.

A minimum of deformity results following treatment of a large protruding carcinoma by radiotherapy, due to conservation of surrounding normal tissues. None of the 7 irradiated cases necessitated plastic repair. One case (Case III) has an ectropion which might be improved by a plastic procedure.

I wish to express my indebtedness to Dr. J. P. Tollman, Associate Professor of Pathology at the University of Nebraska College of Medicine, for interpretation of microscopic sections and preparation of photomicrographs.

SUMMARY

1. Large protruding carcinomas occurring in the basal cell areas frequently show the alveolar or adenoid arrangement of basal cell lesions combined with keratinizing features, simple adenoid epithelioma of Ewing.

2. Bulky squamous cell carcinomas tend to be moderately to highly anaplastic and show an abundant delicate vascular network which is associated with moderately high radiosensitivity.

3. The prognosis is reassuringly good since metastases to regional lymph nodes are remarkably infrequent, in view of the size and activity of the primary lesion.

4. Deformity following eradication of the neoplasm by irradiation is surprisingly little due to only superficial invasion of healthy tissues by the neoplasm.

5. The tumors can be successfully treated by roentgen rays, radium, surgery or a combination of these agents, according to the individual problem or in keeping with the equipment and experience of the therapist.

6. In general we would favor in:

   a. Grade I carcinoma and radioresistant papillary tumors in general, and large tumors overlying the brain: surgical resection and plastic repair.

   b. Pendulous or polypoid carcinoma: irradiation of the base after removal of protuberant portion.

   c. Usual sessile protruding tumor: preliminary roentgen rays followed by interstitial irradiation in the remnants of the base if and as indicated.

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DISCUSSION OF PAPERS OF DRS. CAMPBELL AND HUNT

Dr. Robert E. Fricke, Rochester, Minn. This has been a splendid series of papers. I think Dr. Campbell's paper on photography is most stimulating. I am sure a good colored transparency is worth a page of descriptive records. We have for years been taking colored slides of interesting lesions, especially hemangiomas in children or telangiectasis of the skin resulting from irradiation or things of that kind.

I have tried photography of the cervix but have not been nearly as successful as Dr. Campbell. I am sure we have all picked up some interesting points. We have been placing the patient in the knee-chest position and using a different sized tubular speculum with two lights near the base; we have obtained some fairly good color photographs and movies but those that Dr. Campbell showed are outstanding. I think the point of standardizing the lights and the distance of the camera is very important.

Dr. Hunt's excellent paper on the treatment of bulky carcinomas applies also to gynecologic practice. It was my fortune in the early twenties to work for some years with Dr. Howard A. Kelly and Dr. Burnam in Baltimore and I could predict the approach of these men to the problem of treating a bulky, everting carcinoma of the cervix; Dr. Kelly with primary surgical training would always remove the bulk of the growth with the cautery or endotherm current and treat the base of the growth; Dr. Burnam would insert radium as we do now, at The Mayo Clinic, right into the growth and use it as filtration to protect the normal tissues. The end-results were usually good in both cases but we would rather treat these bulky growths than the infiltrating variety.

Dr. Charles L. Martin, Dallas, Texas. Our histological experience parallels that of Dr. Hunt. On several occasions a biopsy from one portion of a cancer of the skin has been reported as basal cell carcinoma and from another portion as squamous cell carcinoma. And, for this reason, our technique for all the larger cancers of the skin is intensive. I wish to compliment him on the excellent results which he has shown and to ask him to say a little more about his technique for the treatment of metastatic cervical lymph nodes. A survey of our own cases has led us to believe that a dose of 10 to 13 T.E.D. is needed for the control of squamous cell cancer in lymph nodes, but we have been unable to safely deliver such a dose to the neck with 200 kv. roentgen rays alone.

Dr. John E. Wirth, Baltimore, Md. I think if any of the members have attempted to take photographs of the cervix they will appreciate the photographs that appeared here today. I don't know how many different gadgets I have tried for this and none have been particularly successful.

There is one thing I would like to get straight however, from Dr. Campbell. What is the exact arrangement of these lights in taking photographs of the cervix? Do I understand correctly that there are two lights attached to the speculum and those two small lights supply all of the light for the taking of these pictures?

Dr. Hunt's work is extremely spectacular and not too unusual in the sense that I believe a great many of us see these large, bulky lesions and they represent the types of cases that probably keep up our hopes in the treatment of cancer.

Dr. Campbell (closing). I just want to close by saying that cervix photography is an office procedure that can be done in one or two minutes' time with no inconvenience to the patient. I have a speculum here and all of the

lighting is supplied by these two small lights. They have a Weston meter reading of 12 and give a sufficient whiteness or color temperature to closely approach that of a photoflood to which Kodachrome "A" is adjusted.

The maintenance of the proper color temperature in the lights is vital to the accurate rendition of color in the transparency and the proper colors are only obtained when this is around 3,400 Kelvins.

Dr. G. Failla, New York City. May I ask how many hours the lights last?

Dr. Campbell: I have used these same lights for three weeks and have taken perhaps fifty pictures with them. One must watch the color temperature of the filaments, for in some lights this decreases very rapidly with use. In order that the lights burn at this high color temperature as short a time as possible, the routine examination of the cervix and the focusing is done with a much lower rheostat reading. When this is accomplished the rheostat is turned to the proper predetermined setting which gives the correct color temperature and the picture is taken. Excessive heating of the lights is not present if the above procedure is employed, for we have had no complaints from our patients in this regard.

Vol. 44, No. 2

CARCINOMA OF THE ANUS

ITS INCIDENCE, PATHOLOGY AND RADIATION TREATMENT*

By IRA I. KAPLAN B.Sc., M.D., *and* SIDNEY RUBENFELD, B.Sc., M.D.
Bellevue Hospital
NEW YORK CITY

EPITHELIOMA of the anus is of such uncommon occurrence that a series of only 8 cases warrants analysis as to the diagnosis and the technique of therapy.

In the Radiation Therapy Service at Bellevue Hospital, we have encountered but 8 cases of primary anal cancer during the past fifteen years. This represents an incidence of 4.6 per cent of rectal cancer, and 0.13 per cent of all cases of cancer seen in our service since 1924. Of these 8 cases, 6 were in males and 2 in females.

As always in the realm of etiology in malignant tumors we possess no definite information. The factor of chronic irritation hardly plays an important rôle in any of the cases here reported nor were hemorrhoids, fissures or fistulae listed as antecedent factors in any of them.

SYMPTOMATOLOGY

The diagnosis of a lesion in so accessible an anatomic location rarely presents difficulties. The symptoms were sharply defined in this series: 4 of the patients had pain on defecation as the dominant symptom, and 4 felt a growth protruding from the anus. A mass in the inguinal region was present along with the symptom of pain on defecation in one patient. Another patient had observed pencil-like stools, but did not present this as a primary symptom.

The pain was sharp and lancinating in character, always present during defecation, and in 2 individuals it was present constantly.

The physical clinical findings are invariably characteristic, readily enabling a diagnosis to be made. There may be an ulcerated papillary mass extending from one part of the anus or encircling the entire ring. More commonly, however, there is a hard nodular infiltrative mass involving the anus and yielding a rigid, non-flexible ring (Fig. 1). An ulcerated lesion will present a raised rolled whitish edge, although

FIG. 1. This lesion presented as a nodular infiltrative, indurated mass involving the entire circumference of the anus yielding a rigid, inflexible ring.

this finding may well be present in benign ulcerations (Fig. 2). A lesion which has progressed will present an indurated, infiltrative, ulcerated mass extending into the rectum or even into the soft parts of the buttocks. Due to secondary infection, pain, tenderness and tenesmus are prone to be present; bleeding also appears as a major symptom at this stage. The inguinal glands are involved usually late in the course of the disease. In this series, 2 patients had palpable large nodes.

DIAGNOSIS

Histological examination of a biopsied specimen is the only positive way of establishing a diagnosis. However, in the early stage there may be difficulty in differentiating it from benign lesions. Among

* From the Radiation Therapy Service of Bellevue Hospital, Ira I. Kaplan, Director. Read at the Thirty-Ninth Annual Meeting, American Roentgen Ray Society, Atlantic City, N. J., Sept. 20–23, 1938.

Fig. 2. Illustrating a circular, cauliflower lesion growing about the entire ring of the anus, and presenting a characteristic malignant induration.

the latter should be mentioned tuberculosis which often has a concomitant lung infection; fissures and fistulae of long duration, which may become scarred because of chronicity; venereal condylomata, which may be ruled out by serological tests. Often, however, only a histological study will be of aid in determining the character of the lesion.

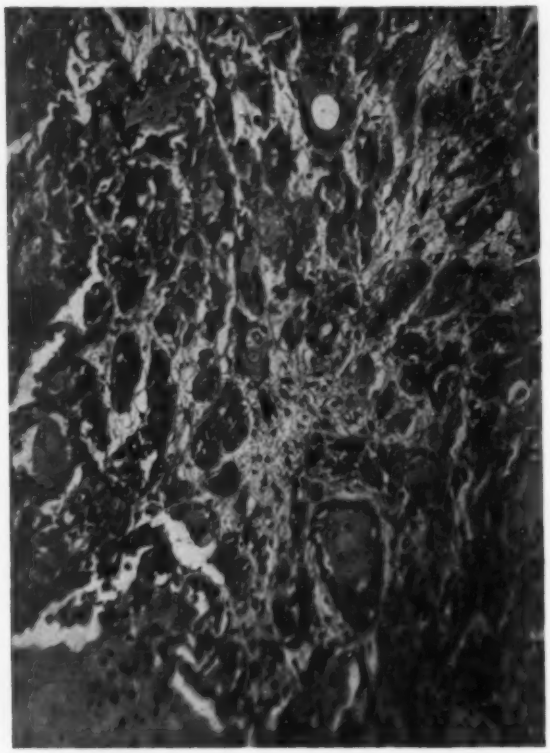

Fig. 3. Low power view of section from lesion near external sphincter. Highly keratinized adult squamous cell epithelioma with pearl formation in a loosely woven stroma.

Distinction must be made from a neoplasm involving the anus as extension from a neighboring growth. We have seen anal involvement as a direct extension of vulval, scrotal or penile cancer; a rectal carcinoma may infiltrate and involve the anus.

Fig. 4. High power section from a lesion high up in the canal, showing a cellular mass of immature epithelial cells.

PATHOLOGY

The anal part of the rectum is divided anatomically into three parts: the columnar, intermediate and cutaneous zones. The epithelium in the columnar zone shows a gradual transition from the rectal mucosa to a two- or three-layered simple columnar epithelium. In the upper part of the zone several intestinal glands may be found.

From the columnar to the intermediate zones, the epithelium changes abruptly to a squamous type. The anal canal is a general anatomical term referring to that part of the terminal intestine beyond the linea ani rectalis and levator ani muscle. Since the proximal part of this anatomical division has simple columnar epithelium and intestinal glands, adenocarcinoma may arise therefrom. Malignant tumors originating from the two distal zones will usually prove to be squamous cell epithelioma. Also, depending upon the point of origin, there may be a highly keratinized low grade epithelioma arising from near the skin margin (Fig. 3), or more cellular anaplastic epithelioma arising higher in the canal (Fig. 4).

In our series of 8 cases, 4 were of the squamous cell type and 4 of the glandular type of malignant neoplasia.

METASTASES

The lymphatic drainage from the anus is to the inguinal glands via channels which run forward in the crura scrotal region. An inferior group of glands drains the margin of the skin about the anus directly into the inguinal glands. A middle group drains the ano-cutaneous region and empties into the inguinal chain.

TREATMENT

The therapy of cancer of the anus, whether surgery, irradiation or a combination of both is indicated, will often depend upon the judgment of the individual therapist rather than on the dictates of standard therapy. This is quite understandable in view of the variations in cures thus far obtained. Colostomy, in our opinion, is required only when complete obstruction occurs or when, even with bowel hygiene, pain on defecation is totally unbearable. Treatment begins with irradiation of the inguinal lymphatics and this is carried out simultaneously with treatment of the local area when roentgen therapy is used for the latter. Where the inguinal nodes are definitely palpable, discrete, and freely movable, they may be treated with roentgen therapy and then surgically removed. Where any surgical procedure is contraindicated, irradiation alone is employed. Limiting our discussion primarily to radiation therapy, it is interesting to note that the various techniques employed even in this small series evidenced the efficacy and shortcomings of each.

Case C. D. presented an anal lesion which microscopically showed a transitional cell epithelioma. By means of a proctostat,* radium therapy was administered for a dose of 6,000 mg-hr. There ensued the customary radium reaction, which subsided with a total disappearance of the tumor mass. Three months later the patient succumbed to an attack of lobar pneumonia. At postmortem examination careful search of the lower rectum and anus failed to disclose any neoplastic areas.

In contradistinction to the above case where radium tubes were inserted in a rubber container, another patient, R. H., presented a fissured mass in the anus which was histologically proved to be squamous cell epithelioma. Ten platinum filtered radium needles were inserted radially about the anus administering a dose of 2,400 mg-hr. At the end of eight weeks following treatment, no tumor was palpable or visible. It is evident, therefore, that in selected cases, interstitial as well as topical radium application is well indicated.

Of the 8 cases, only one survived the accepted five year period. So far as local tumor response is concerned, the squamous cell tumors proved to be far more sensitive than the adenocarcinomas. In 4 patients with squamous cell growths, where radium was the direct attack on the local lesion, there was a total disappearance of the primary growth in all cases.

* The proctostat is a special rubber tube device for the application of filtered radium to the anal and rectal canal. It consists of a thick molded soft rubber tube applicator with a central hollow core to allow for drainage of bowel fluids, cleansing, and escape of bowel gas. The inserted tip is of soft rubber and the rear end has a hard rubber connecting tip to permit attachment to an enema bag or additional drainage tubing, should the applicator be placed high up in the rectum. The outer shell of the proctostat is fenestrated at equal distances to hold nine radium tubes. After the radium tubes are set in place a protective thin rubber sleeve is rolled over the proctostat, holding the radium tubes in place. When the applicator is ready for insertion into the rectum it is wound in puttee style, with a strip of iodoform gauze, which is split into two streamers and tied about the end of the tube; the lower ends of the streamers are then used to anchor the tube in place by attachment to the buttocks with adhesive tape.

Fig. 5. Roentgenogram illustrating the radical manner in which needles of 60 mm. length, filtered through 0.6 mm. of platinum are inserted about the anus. A proctostat containing tubes is also visible.

In the light of our experience based even on this small series, the following procedure is recommended for the treatment of carcinoma of the anus:

A. Cases without Inguinal Gland Involvement. The anal lesion may be treated by direct roentgen therapy using 200 kv. potential and a filter of 2 mm. Cu when daily doses of 150 to 200 r are administered. The nature of the response should be noted, and if at the end of a dose of about 2,000 r there is satisfactory reduction in the size of the tumor, the same mode of therapy should be continued until at least 4,000 r are delivered. The histological variants determine the radiosensitivity of the tumor. A keratinized adult neoplasm obviously will show a less rapid recession than a cellular plexiform epithelioma. For this reason a trial dose of roentgen radiation must be given to determine the tumor response.

If the neoplasm proves resistant to this technique, roentgen treatment is stopped and radium therapy employed. Interstitial therapy with platinum filtered needles is the method of choice. With the anal canal well relaxed radium needles are inserted radially about the anal canal to surround the lesion. The finger inserted in the anal canal will yield information as to the upward extent of the induration and this will determine the length of radium needles to be employed. The dose may vary but there should be no hesitation in giving about 1,000 mg-hr. per cubic centimeter (Fig. 5).

If one is hesitant about placing puncture needles in the lesion, then the proctostat offers the best means for topical application of radium.

Radium tubes of 5 or 10 mg. content are used and sufficient time utilized to yield a dose of 4,000 to 5,000 mg-hr. The filter should be at least 1.5 mm. of platinum or its equivalent.

B. Cases with Inguinal Gland Involvement. Unless surgically removed the radiosensitivity of a metastatic inguinal gland cannot be accurately defined. It is wise therefore to administer a trial roentgen-ray dose of sufficient magnitude to note the response to irradiation before any more radical attempts are made for treating such metastasis. For this trial, we suggest 200 kv. potential with 0.5 to 1 mm. Cu filter. A dose of 1,500 to 2,000 r in daily treatments is administered. If no response is evident, roentgen therapy should be stopped and surgical dissection of the glands performed.

The presence of metastatic nodes does not alter the mode of therapy to the local lesion.

Modifications in this procedure are required when there are huge, bulky lesions. One that is annular and obstructs the anal opening may necessitate a colostomy prior to any irradiation. A massive papillary outgrowth should first be resected by surgical diathermy before roentgen or radium therapy is instituted.

The reaction that follows radium treatment is often severe and distressing. Daily cleansing, enemas, opium and belladonna

suppositories, and a bland ointment such as aquaphor to the skin edges, olive oil instillations, all these incidental cares will greatly alleviate pain and hasten subsidence of the reaction.

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DISCUSSION

Dr. Robert E. Fricke, Rochester, Minn. Dr. Kaplan and Dr. Rubenfeld have presented an excellent and detailed study of this interesting condition. Our experience at the Mayo Clinic in the diagnosis and treatment of this fortunately rare malady has closely paralleled that of Dr. Kaplan and Dr. Rubenfeld, so my discussion will be mainly to emphasize some of the points which they have brought out.

I think the points worthy of emphasis are the fortunate rarity of this disease, the necessity for biopsy, the bad prognosis, the study of the pathology, and the lack of any standardized method of treatment.

In his "Practical Proctology," Buie also found a very low incidence in all the patients seen at the Mayo Clinic over a thirteen year period. Of 51 patients studied, he found 90 per cent on microscopic examination to be squamous cell epithelioma, and the prognosis was bad in all. The primary cases yielded rapidly to radium treatment or excision, but metastasis was widespread, first to the inguinal nodes.

During this year, we have had 7 patients with carcinoma of the anus referred for radium therapy. One of these had had many operations and treatments over a period of years, with much scarring. Tissue was not obtainable. In the remaining 6, all were squamous cell epithelioma, one mixed with adenocarcinoma and one mixed with basal cell elements. Three were low grade and three high grade (3 and 4). In all these, gross lesions varied greatly and the treatment was highly individualized, as suggested by Dr. Kaplan.

In 5 of the 7 cases, topical radium was applied by a central applicator of rubber containing radium tubes. No needles or seeds were used in these cases, although we have used them in the past. The treatment consisted mainly of topical application of tubes to different parts of the lesion daily, giving 90 to 100 mg-hr. per square centimeter of tissue and in the majority of cases the inguinal nodes were treated with radium packs.

Another important point indicated by Dr. Kaplan and Dr. Rubenfeld is the importance of the after-care in these patients. These lesions are exquisitely painful due to their location and every effort must be made to keep these patients as comfortable as possible during the period of reaction from the treatment and after.

Fortunately, primary malignancy of the anus is very rare. During thirteen years, from 1920 to 1932, of all patients having proctoscopic examinations at the Mayo Clinic, only 51 had anal cancer, an incidence of 0.08 per cent. In the same group, there were 2,939 cases of carcinoma of the anus, rectum or sigmoid. The incidence of anal epithelioma was 1.73 per cent of all malignant rectal lesions. Only one was adenocarcinoma, probably due to an involvement of the sweat gland. Of the 51 patients, approximately half were males and half females. The symptoms were chiefly pain, a good deal as in the case of a fissure. The symptoms were often disguised by the taking of laxatives to soften the stool. Other symptoms were the early appearance of blood, constipation, a feeling of fullness in the rectum, anal discharge, soreness and irritation.

The gross appearance varies a great deal. Biopsy is usually necessary. On microscopic examination, 90 per cent were squamous cell epithelioma, with occasionally a basal cell type. Of the 51 patients, there were 6 of Grade 1, 10 of Grade 2, 21 of Grade 3 and 6 of Grade 4. In the majority of cases, the inguinal nodes were palpable and also were treated with external irradiation. From our past experience, we do have hopes of good effect in the Grade 1 and 2 lesions but the Grade 3 and 4 are usually a hopeless proposition; not that the primary lesion does not regress but the incidence of distal metastasis is high in these lesions.

PHYSICAL DIFFERENCES BETWEEN TYPES OF PENETRATING RADIATION*

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THE unexpected discovery of the value of roentgen rays and radium for treatment of cancer emphasizes the importance of examining the characteristics of the more recently discovered types of radiation. Experience indicates that radiations that are to be useful for tumor treatment must be ionizing rays. We may thus neglect those rays, such as infra-red and radio rays, which have a wave-length longer than light and consider only those of shorter wave-length. Ultraviolet light is too rapidly absorbed to be considered as an agent for other than surface treatment. Of the more penetrating ionizing rays, roentgen rays, i.e., light of very short wave-length, are the most familiar. We must accordingly consider the relative effects of roentgen rays of different wave-lengths or voltages. In addition, however, there are various types of corpuscular rays which are likewise penetrating when they have sufficient energy. Among these corpuscular rays are the familiar electrons, which we know as cathode rays and beta rays, and the less familiar alpha rays, protons, neutrons, deuterons, positrons and mesotrons, not to mention the neutrinos and neutrettos whose existence is perhaps still questionable. Our present problem is to interpret the physical properties of these various rays in such a manner as to indicate their probable therapeutic value.

We can quickly dispose of most of the less familiar radiations. There is one group which consists of fast moving atomic nuclei. These are the protons, deuterons and alpha particles, the nuclei of hydrogen, heavy hydrogen, and helium respectively. In order that these rays may have a penetrating power comparable with roentgen rays, their energy needs to be immensely greater than present technique can impart, of the order of hundreds of thousands of kilovolts. It is probable that at such energies their properties might make them of practical interest. But this lies in the distant future.

Positrons, or positive electrons, are found to act in a manner very similar to the familiar negative electrons, except that they may attach themselves to negative electrons and spend themselves in the production of a penetrating gamma ray. Positrons thus have ionizing and penetrating powers intermediate between those of electrons and gamma or roentgen rays.

Most penetrating of all known forms of radiation at very high energy is the mesotron, a newly discovered component of cosmic rays. The mesotron is a particle with either a positive or a negative charge, of the same magnitude as that of an electron, and with a mass when at rest of about one-tenth that of a hydrogen atom. The mesotron's exceptional penetration appears only when its energy is over a hundred million electron volts. At present we know of no artificial method of producing these rays, and their intensity in cosmic rays is far too feeble for therapeutic use. Furthermore, their ionizing properties are found to be so similar to those of high speed electrons that they would seem to be of no unusual therapeutic interest.

Of the available types of penetrating radiations, this leaves us with roentgen rays (or gamma rays), electrons (or beta rays), and neutrons. The two chief physical characteristics of these rays with which we are concerned are their penetration and their method of ionization. The meaning of dif-

* Read at the Fortieth Annual Meeting, American Roentgen Ray Society, Chicago, Ill., Sept. 19–22, 1939.

ferences in penetration, as measured, for example, by their absorption coefficients, is too familiar to require elaboration. It may be worth while, however, to explain what is meant by differences in the method of ionization.

I presume you have all read of, if you have not seen, the cloud chambers with which photographs are made of the tracks of ionizing particles. Figure 1 shows such a glass-walled cloud chamber filled with a fog condensed on ions produced by a mixture of gamma rays and neutrons. Two distinct types of tracks will be noted, heavy white tracks in which the individual droplets are too close to be distinguished, and thinner, more diffuse tracks, where the individual droplets can be seen. These tracks represent respectively the protons which are formed by the neutrons, and the electrons which the roentgen rays excite. Neither neutrons nor roentgen rays produce ionization directly. It is thus evident that neutrons produce ionization in much more concentrated regions than do roentgen rays. In view of this marked physical difference in the mode of ionization, therefore, it would not be surprising to find a distinctive biological action of the two types of rays.

There is a similar, though less striking contrast between the concentration of ions produced by slowly and rapidly moving electrons. The number of ions per centimeter path of the electron is in fact inversely proportional to the square of the speed with which it moves. This means that low voltage electrons produce more concentrated ionization than do high voltage electrons. When the electron's energy is as great, however, as 200 electron kilovolts, it is already moving with a speed so close to that of light that additional energy does not appreciably change its speed, and the ions along the path do not spread out any more. It follows that with regard to ion density, no important changes in the properties of electrons occur for energies greater than about 200,000 electron volts.

Cathode electrons at voltage available in the laboratory are too easily absorbed to be classed as penetrating rays. The tubes would need to be operated at potentials of the order of 100 times those now available for them to compare favorably in penetration with the roentgen rays now in use. Nor should we expect such immensely energetic electrons to show ionization characteristics differing appreciably from those of ordinary high voltage roentgen rays. There would thus appear no reason for developing supervoltage electron rays for deep therapy.

Fig. 1. Cloud photographs of tracks of protons (dense white lines) and electrons (thin lines) excited respectively by neutrons and gamma rays (Lawrence).

Neutrons and roentgen rays show much the same penetration in human tissue. Both are sufficiently penetrating to be useful in deep treatment. At present the only type of neutron generator capable of producing neutrons in quantity adequate for human therapy is the so-called "cyclotron," developed by Professor E. O. Lawrence. This consists essentially of a powerful magnet and an electrical oscillator, which serve to produce a high energy beam of deuterons. When this beam strikes a target of beryllium, gamma rays and neutrons are produced, much as cathode rays striking a tungsten target produce roentgen rays. The gamma rays may be removed by a filter of lead, which the neutrons readily penetrate, leaving a nearly pure neutron beam. Fig-

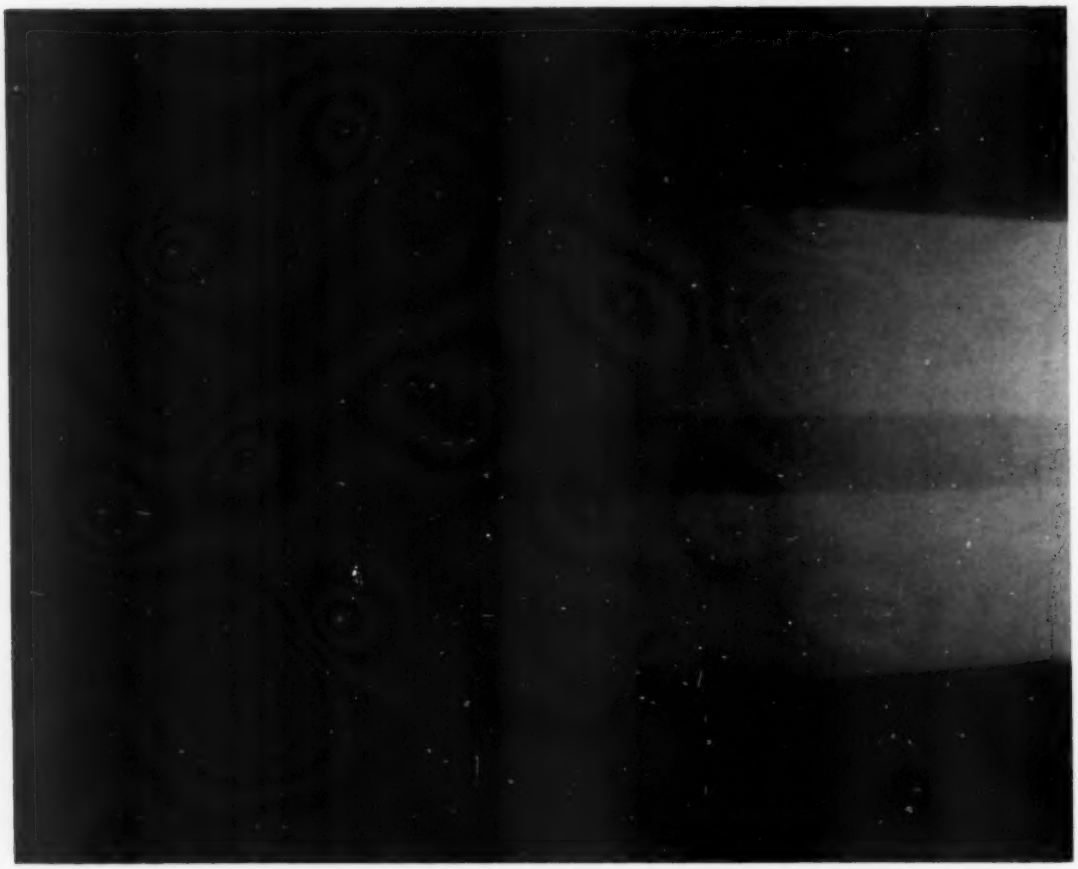

Fig. 2. Photographic impression made by neutron rays after traversing 1 inch of lead. Central shadow cast by 3 cm. of paraffin (Lawrence).

ure 2 is a photograph made by such a neutron beam after passing through the diaphragm of Lawrence's first therapeutic cyclotron. With his latest instrument, shown in Figure 3, weighing some 220 tons and operating at about 100 kilowatts, a beam of neutrons is produced whose biological effect is of the same order of intensity as that of filtered roentgen rays from the usual 200 kilovolt, therapeutic roentgen tube.

While the penetration and the intensity of such neutron rays are closely similar to the high voltage roentgen rays in common use, the neutrons show two significant physical differences. The first of these is that of the much greater concentration of ions along the paths of the protons which the neutrons excite in the irradiated material. The second is that neutrons act much more strongly upon hydrogen-containing substances than upon any other, while for hard roentgen rays hydrogen, having the fewest electrons, is least affected. This marked absorption of neutrons by hydrogen is illustrated by the shadow in the middle of the neutron beam shown in Figure 2. This shadow is cast by a block of paraffin 3 cm. thick, which would hardly affect a roentgen-ray beam which, like these neutron rays, had been filtered through an inch of lead. Since various organic materials differ in their hydrogen content, this may lead to important biological distinctions in the effect of the rays.

It is as yet too early to say whether neutron rays are really preferable to roentgen rays for any kind of treatment. Because of the physical differences just mentioned, however, it would be surprising if some corresponding differences in their biological ef-

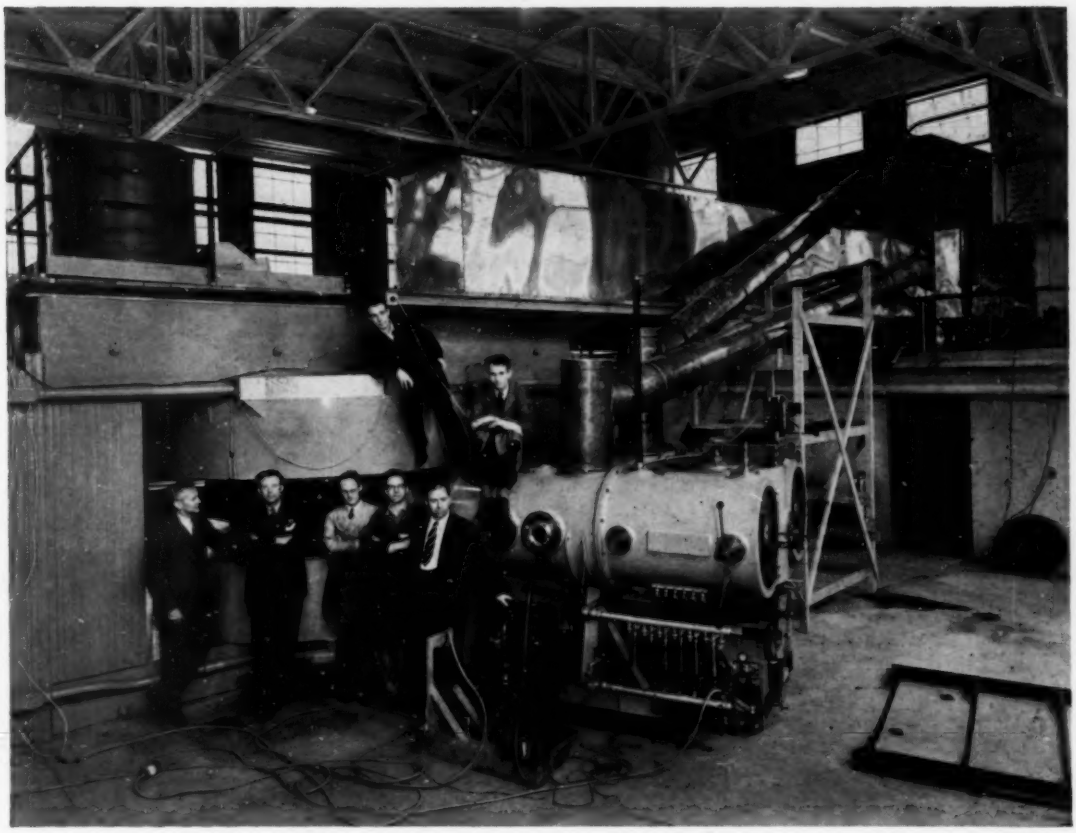

Fig. 3. University of California's 220 ton cyclotron, built for therapeutic purposes, with operating staff (Lawrence).

fects did not appear. Different investigators are not yet in agreement, however, with regard to the magnitude of these biological differences.

There remains the important question as to the physical properties of roentgen rays of higher voltage than now in use. Commercial roentgen-ray equipment of 400 kv. is readily available. A few studies extending over several years have been performed with roentgen rays up to 1,000 kv. Within the last year, Van Atta at Massachusetts Institute of Technology and Bouwers at Eindhoven, Holland, have reported physical measurements with roentgen rays up to about 3 million volts. In cosmic rays we have identified and studied the production, absorption and ionization of roentgen rays excited by electrons of energies between 10 million and 1,000 million electron volts. These studies have made it possible to check and refine the theory of roentgen-ray action. Following are some of the more significant conclusions.

Up to at least several million electron volts, roentgen-ray production continues to increase approximately as the square of the voltage. Over 500 kv. the roentgen rays become strongly concentrated in the general direction of the roentgen-ray beam (Fig. 4). Thus, at 2,000 kv., Van Atta and Northrup find about six times as strong radiation in line with the cathode rays as at right angles. This indicates that the supervoltage tube should be designed in a different manner from the tubes of more moderate voltage.

Van Atta find that in lead the penetrating power of the roentgen rays continues to increase up to 2.5 million volts, whereas in organic material, Bouwers finds a maximum penetration at a little more than 1 million

volts. That is, in human tissue it seems that 3 million volt roentgen rays are less penetrating than 2 million volt rays, and hardly more penetrating than 1 million volt rays. The physical reason for this upward rise in the absorption for very high voltages is well

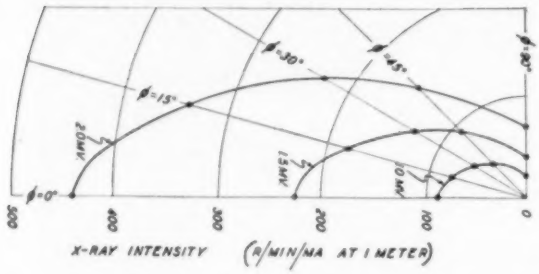

Fig. 4. Variation of roentgen-ray intensity with azimuthal angle at 1.0, 1.5, and 2.0 million volts (Van Atta and Northrup).

understood, but must not be discussed now. Packard of Columbia has recently reported that when the effect of scattered rays is taken into account, he finds the penetration of 700 kv. roentgen rays almost as satisfactory as those at 900 kv. This is clearly indicated by his curves shown in Figure 5. Stone of California goes yet farther, showing that if a patient is irradiated from both sides, 400 kv. roentgen rays give just as high a ratio of depth to surface dosage as do his 1,100 kv. roentgen rays. These studies make it clear that with regard merely to penetrating power, little if anything is to be gained in human therapy by using voltages over half a million, and that even here the advantage over 200,000 volts is less than has frequently been supposed.

It has already been noted that at the higher voltages the ionization along the electron paths is less concentrated, but that the spacing between the ions does not increase much for electron energies over 200 kv. We must remember, though, that the recoil electrons have a much lower average energy than the photons which produce them, and these in turn have less energy than the cathode electrons in the roentgen tube. Thus, to produce recoil electrons with an average energy of 200 kv. requires cathode rays of about 2,000 kv. This means that there is a physically measurable increase in the diffuseness of ion production as the roentgen-ray voltage used increases from 200 to 2,000 kv.

In view of this difference, an observation of Stone becomes of special significance. He showed that when roentgen rays of 200 and 1,200 kv. are accurately controlled to the same dosage, their physiological effects on opposite halves of the same patient could not be distinguished. That is, changes in the diffuseness of the ions, which I estimate to be in the ratio of about 6:1, do not produce detectably different physiological effects. It, of course, remains possible that the 100 fold difference between the concentration of ions produced by neutrons and hard roentgen rays might be very appreciable. This would appear at present to be the most hopeful suggestion from the physical considerations that I have been presenting.

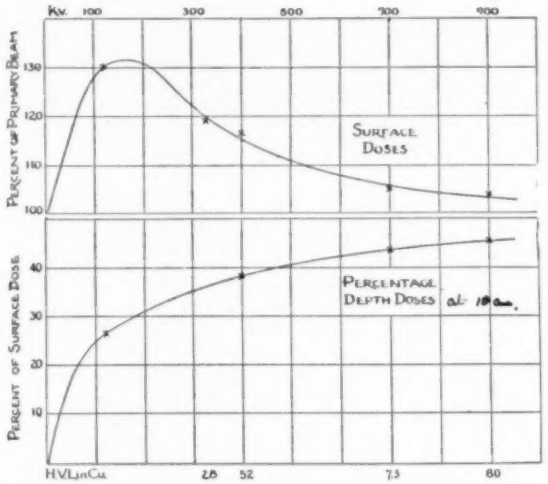

Fig. 5. Curves showing the surface and depth dosage with roentgen rays at potentials of from 100 to 900 kv. (Packard).

While it does not come strictly within the subject of penetrating radiations, this discussion would not be complete without mentioning the possibilities that have recently been opened by the production of artificial radioactive elements. Most interesting from the therapeutic standpoint are perhaps radio sodium, potassium, iodine, and phosphorus. These can be injected into

the blood stream, or taken as food, and are in certain cases absorbed by the affected tissue. Where this can be done, it makes possible local irradiation under ideal conditions. Qualitatively, however, the effects of the irradiation from such substances will presumably be identical with those of roentgen rays or radium as ordinarily applied.

Of the available forms of penetrating radiation, therefore, the only ones whose physical properties give promise of valuable therapeutic properties are roentgen rays and neutrons. Studies made with roentgen rays up to very high voltages indicate that nothing is to be gained with regard to penetration or nature of the ionization by going to potentials over about 500 kv. Neutron rays are of about the same penetrating power as such roentgen rays, but differ in that the ions they produce occur in highly concentrated groups, and in their preferred action on hydrogen bearing matter. Because of these physical differences, differences in the biological effects of the two types of rays should appear; but it is not yet known under what condition, if any, neutrons are superior in their therapeutic action to roentgen rays. This, however, is evidently a hopeful field of experimentation.*

* For discussion see page 284.

INTERSTITIAL RADIUM DOSAGE EXPRESSED IN ROENTGENS*

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THE expression of radium dosage in milligram-hours or millicuries-destroyed is inadequate, because the dose within a lesion, which determines the biologic effect, is not defined by the amount of radium used and the time of its application. In 2 cases, in which the same amount of radium is applied for the same time, there may exist a considerable difference in the amount of radiation which is absorbed in an equal volume of tissue, depending on differences of spatial distribution and of filtration. Addition of these varying factors of distribution and filtration to the milligram-hours may render a certain tissue dose reproducible under exactly the same conditions, but it does not make comparable two doses given under different conditions.

After many years of work to develop an ionization unit for gamma radiation the International Committee for Radiological Units proposed at the Fifth International Congress of Radiology in 1937 the adoption of the unit for roentgen rays, the roentgen, r, also for gamma rays. The realization of the roentgen in the range of gamma rays has been tried in different ways. The method of calculating it from ascertained physical data and measurements with small air-wall ionization chambers have led to a satisfactory agreement. A value of about 8.4 r for the standard dosage rate of 1 mg-hr. at 1 cm. distance from a point source filtered with 0.5 mm. Pt is thereby obtained. But the problems of clinical radium dosage in roentgens are still far from being settled by these agreements.

Because of the very rapid decrease of the radiation intensity around a radium source the direct measurement of dosage at the surface and in the immediate neighborhood of radium foci and in a given point is limited, at least as long as chambers of several millimeters in diameter are used. Besides, in radium therapy we do not always deal with gamma radiation under conditions in conformance with the definition of the roentgen. For the solution of these problems in the direct ionization measurement of tissue dosage, Failla has developed the extrapolation chamber. But measurements with it are not yet available for clinical radium dosage.

For the use of the radiotherapist, formulas, charts and graphs have been worked out after laboratory measurements of the standard mg-hr./cm. by calculation, of which the dosage system by Paterson and Parker is the most complete. It supplies for interstitial as well as for surface dosage curves, showing the milligram-hours necessary to produce 1,000 r minimum dosage in different volumes of tissue under stated conditions. According to Parker, the absorption and scattering of gamma radiation in the tissue does not exceed 4 per cent and may be neglected at least for distances up to 3 cm. in calculating the dosage distribution in tissue. Several factors, however, such as lack of homogeneity of the medium, additional ionization by secondary rays from the filters, absorption of radiation in the radium compound itself and difficulties in determining the exact filtration at the ends of the needles, limit also to a certain degree the method of calculating interstitial dosage.

Before the mathematical method was developed clinicians used other radium effects than ionization of gases for direct radium dosage measurements, such as radiochemical processes and biological reactions, which are widely based on and parallel to ionization effects. They con-

* Read at the Fortieth Annual Meeting, American Roentgen Ray Society, Chicago, Ill., Sept. 19–22, 1939.

tinue to be valuable, where other methods are limited.

In interstitial radium therapy, Failla, Quimby and their coworkers were the first to check the dosage distribution around radon seeds by a butter bleaching method and to use the threshold erythema dose as a reproducible dosage unit. A very comprehensive system for interstitial radium dosage was worked out by them and laid down in tables furnishing the milligram-hours or millicuries-destroyed necessary for different numbers of threshold erythema doses under varying conditions of application.

In Holthusen's clinic in Hamburg the blackening of the photographic layer is used for direct measurements of radium dosage and the dosage expressed in r-equivalent units. The essential part of the method, on which several publications have appeared since 1932, is that two series of films are exposed to radium, one series at the place where the dosage rate is to be measured, under a surface mould or in a phantom between inserted radium needles, the other series under standard conditions to a standard tube of radium, the dosage rate of which in this standard arrangement has been calibrated by ionization measurement in roentgens. Both series of films, cut out of the same film emulsion, are developed simultaneously to guarantee equal conditions of handling. By photometric comparison of the blackening of the test films and the standard films the tested dosage rate also is expressed in roentgen-equivalents. The photographic layer lends itself to measurements at the surface of specimens and in small distances, its blackening being proportional to the actual ionization in any point. Its disturbing mass in phantom measurements is small compared with that of ionization chambers. There is no question about the fitness of the photographic method for relative dosage measurements. The calibration in roentgen-equivalents has been checked in the Institute for Radiological Research in Berlin, where also comparisons were made of results of photometric measurements with those of direct ionization measurements, which proved in sufficient agreement for clinical purposes. We do, of course, not ignore the fact, that these r-equivalents are not measured in conformity with the definition of the roentgen. They furnish a reproducible unit of physical dosage, differing from a biological unit as the erythema dose by its independence on the time factor. Years of clinical experience have shown that its therapeutic value corresponds closely to the roentgen as defined for roentgen rays so far as the reactions and effects of equal numbers of units of both kinds are equal, if the conditions of application regarding the distribution in time and space are equal.

As a clinician I present the following tables on interstitial radium dosage in roentgen-equivalents, though they are of limited use, being worked out for special types of needles and relatively small volumes only, for two reasons:

1. There exists only a relatively small number of publications on comparisons of radium dosage expressed in roentgens based on calculation with empirical dosage and with the results of direct measurements. Most of the latter that have been made are restricted to the dosage distribution around single specimens or special applicators. This contribution may suggest further comparisons of dosage in larger volumes of tissue, which appear highly desirable.

2. In the use of our dosage table some points are of less strict consideration than in the application of the curves of Paterson and Parker. Not all lesions lend themselves to the geometrical forms of implantation, for which the Manchester graphs are provided. Our distribution is less strictly geometrical. If the radium supply differs greatly from the Manchester supply, which consists of a great variety of needles, part of them of uncommonly low linear intensity, the dosage becomes very inaccurate. Our needle supply was limited to two common types of 1 and 2.5 cm. active length.

The measurement of the implanted volume is by no means easy and inaccuracies produce very serious miscalculations of dosage. We assess it by a simple approximation.

The tables are based on different series of measurements.

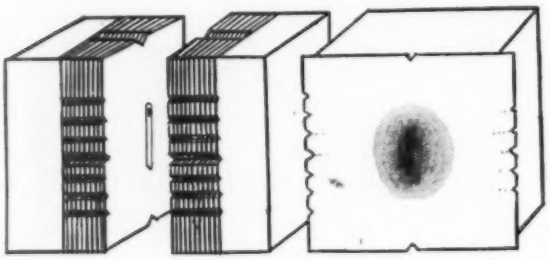

Fig. 1

I.A. The first was made in a wax phantom of 10 cm. diameter, consisting of layers of 2 mm. thickness, around single needles. The measurements were performed in planes at right angle to the axis of the needles, the plane through the center of the active length and in parallel planes in 5, 10 and 15 mm. distance, in distances 0–20 mm. from the needle surface (Fig. 1).

B. From the mean values of these measurements the dosage was calculated for the routine insertion of needles for volumes of about 5–50 cc. and the use of 3–20 needles. The minimum, maximum and average dosage was calculated (a) for one hour, (b) for the empirical dosage in interstitial cancer treatment, formerly expressed in milligram-hours or millicuries-destroyed.

In the other series the calculated dosage was checked by measurements, in

II.A, in a second wax phantom of 9 cm. side length, consisting of layers of 1 mm. thickness, between 10 needles in typical distribution (Fig. 2);

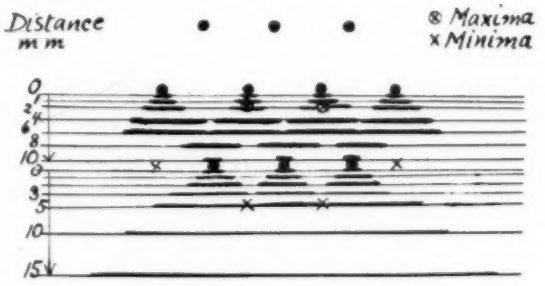

Fig. 2

B, in a third wax phantom of 10 cm. side length in four planes, one oblique and three parallel to the needles, between 10 needles of different active length (Fig. 3), and

Table I

DISTRIBUTION OF RADIATION AROUND TWO DIFFERENT TYPES OF NEEDLES

Radium Active Length Filtration	(a) 3.3 mg. 2.5 cm. 0.5 mm. Pt		(b) 2.0 mg. 1.0 cm. 0.5 mm. Pt	
Percentage of	Dosage rate at the surface = 2.4 r per min.	at 2 mm. dist. = 1 r per min.	at the surface =3.5 r per min.	at 2 mm. dist. =0.97 r per min.
Distance from the surface in mm.				
0	100.0	240.0	100.0	360.0
2	45.0	100.0	27.8	100.0
4	28.8	64.3	12.8	47.4
6	20.0	41.2	9.8	35.2
8	12.0	26.0	5.6	20.2
10	7.2	16.4	3.6	13.4
15	4.3	9.5	1.9	6.9
20	2.5	5.5	1.1	4.1

III, in the same spatial distribution as under II.B in tongues of cadavers, (A) in situ, (B) in isolated tongues.

Ad I.A. *Distribution of dosage around single needles* (*Table I and Fig. 4*):

The needles used for the measurements were of two types, both filtered with 0.5 mm. Pt (a) of 3.7 cm. total length, containing 3.3 mg. radium in 2.5 cm. active length, that is 1.32 mg. per active cm., (b) of 2.7 cm. total length, containing 2.0 mg. radium in 1 cm. active length, that is 2 mg. per active cm.

The values for the dosage rates at the surface and at 2 mm. distance are the mean values of measurements with each needle of the whole supply at that time, the dosage rates in greater distances the mean of the measurements with 5 needles of each type.

The dosage is correct in the central plane in right angle to the needle axis. The decrease in dosage in corresponding points of the parallel plane in 1.5 cm. distance in series (a) and 1 cm. distance in (b) does not exceed 20 per cent in distances up to 20 mm. from the axis.

In case (b), 2 mg. per cm. active length, the dosage rate at the surface is about 50 per cent higher than in case (a) and its decrease with the distance more rapid. In 2 mm. distance from the surface the absolute dosage rate of the 2 needle types is practically equal, about 1 r-equivalent per min. The difference in the decrease of intensity is most pronounced in the first 5 mm. At 4 mm. distance the dosage rate is more than a quarter of the dosage rate at the surface in case (a) and less than one-eighth in case (b), or more than two-thirds and less than one-half of the dosage rate at 2 mm. distance.

Because of the additional ionization by secondary beta rays from the filters the dosage values at the surface are not accurate. There are differences of ±15 per cent in our measurements. The values become constant already at 2 mm. distance. Therefore in calculating the average dosage in implants we neglected only the immediate surface dosage, taking the dosage

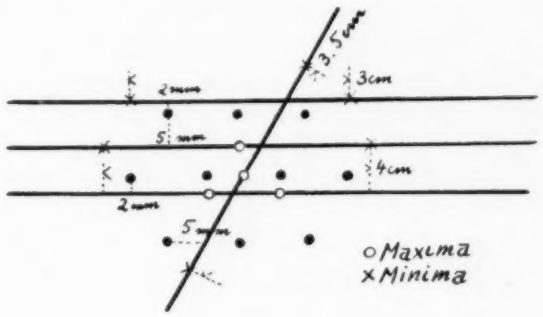

Fig. 3

at 2 mm. distanee as maximum and relating the dosage at greater distances to it as 100 per cent. Regarding the determination of the lethal tumor dose and the tolerance dose of tissue this neglect of the immediate

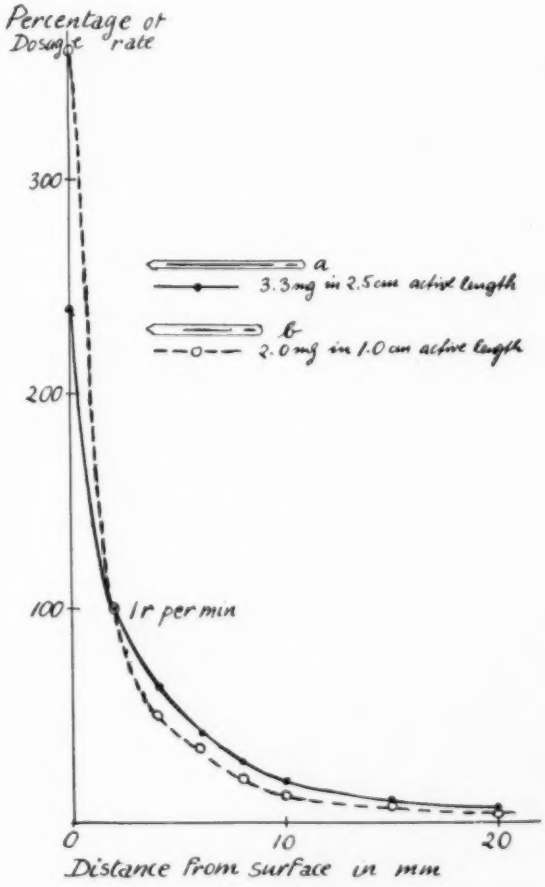

Fig. 4

surface dose seems to be justified. The wall of the channel of insertion is not destroyed

by a selective irradiation effect but by the trauma and a caustic effect of the high surface dose. Besides in the minimum dosage in respect to the minimum lethal tumor dosage we are interested in the average and maximum dosage regarding the tissue tolerance.

The depth of the relatively homogeneously irradiated volume being about 10 mm. greater than the active length, about 10 mm. are added to it, 8 mm. in series (a), 10 mm. in (b). The arbitrary difference simplifies for these two needle types the estimation of the treated volume considerably by making the number of centimeters of one dimension equal to the number of milligrams used. The other two dimensions being about 1 cm. for each needle, provided that they are typically spaced, the total irradiated volume is approximately expressed by a number of cubic centimeters equal to the number of milligrams used.

TABLE II

DOSAGE RATE PER HOUR IN INTERSTITIAL RADIUM THERAPY

	(a) 3.3 mg. needles		
Volume I about 10 cc. 3 needles	Maximum in 2 mm. from surface Minimum Surface of needles	82.5 r 81.6 r 164.0 r	Average 82 r ± 1%
Volume II 13–20 cc. 4– 6 needles	Maximum in 2 mm. from surface Minimum Surface of needles	110.0 r 98.5 r 180.0 r	Average 104 r ± 6%
Volume III 23–36 cc. 7–12 needles	Maximum in 2 mm. from surface Minimum Surface of needles	135.0 r 109.0 r 195.0 r	Average 122 r ± 11%
Volume IV 40–53 cc. 13–16 needles	Maximum in 2 mm. from surface Minimum Surface of needles	156.0 r 122.0 r 218.0 r	Average 139 r ± 12%
	(b) 2.0 mg. needles		
Volume I about 6 cc. 3 needles	Maximum in 2 mm. from surface Minimum Surface of needles	75.0 r 54.0 r 224.0 r	Average 65 r ± 15%
Volume II 8–12 cc. 4– 6 needles	Maximum in 2 mm. from surface Minimum Surface of needles	92.0 r 65.0 r 235.0 r	Average 79 r ± 16%
Volume III 14–20 cc. 7–10 needles	Maximum in 2 mm. from surface Minimum Surface of needles	109.0 r 73.0 r 245.0 r	Average 91 r ± 20%
Volume IV 22–40 cc. 11–20 needles	Maximum in 2 mm. from surface Minimum Surface of needles	122.0 r 82.0 r 250.0 r	Average 102 r ± 20%

Ad I.B. *Interstitial dosage rate in r-equivalents per hour (Table II):*

As typical are regarded volume implants with parallel needles spaced 1 cm. apart and plane implants, in which the distribution may be parallel or end to end according to the rules of best homogeneity lately summarized by Paterson and Parker.

The estimation of the treated volume is based on the active length of the needles.

The same way of approximation in estimating the irradiated volume may of

course be applied for other needle types with different active length and activity, furnishing another numeric relation between milligrams applied and cubic centimeters of treated volume.

The dosage rate increases with the increasing number of needles. Therefore the same dosage is delivered with the same needles in a large volume in a considerably shorter time than in a small one. Under the presented conditions the difference is about 60 per cent between 10 cc. and 50 cc., the dosage rate varying for the type (a) needles between 80 and 140 r per hour and between 65 and 102 r per hour for the type (b) needles.

The difference in the dosage rate of the two types of needles increases considerably with the volume, from 4–26 per cent for the average and from 20–33 per cent for the minimum dosage between 10 and 50 cc. The differences in milligram-hours necessary for 1,000 r minimum tissue dosage are shown later in the curves of Figure 5.

The homogeneity decreases with the increasing volume, the differences between

TABLE III

EMPIRICAL DOSAGE IN INTERSTITIAL CANCER THERAPY EXPRESSED IN ROENTGEN-EQUIVALENTS

3.3 mg. needles

V = volume in cc.	Number of needles	Dosage			
		in mg-hr.	In roentgens		
			Max. surface	Max. 2 mm.	Minim.
I about 10	3	V. 120	16500	9900	9800
				Average:	9850
II 13–20	4– 6	V. 100	16500	11000	8900
				Average:	10400
III 23–36	7–12	V. 90	17100	12100	9500
				Average:	10800
IV 40–50	13–16	V. 80	16900	12500	9300
				Average:	10900
		Mean:	16750	11400	9600
				Average:	10500 ± 10%

2.0 mg. needles

V = volume in cc.	Number of needles	Dosage			
		in mg-hr.	In roentgens		
			Max. surface	Max. 2 mm.	Minim.
I about 6	3	V. 120	26000	9000	6900
				Average:	7950
II 8–12	4– 6	V. 100	27400	8900	6500
				Average:	7700
III 14–20	7–10	V. 90	21700	9800	6300
				Average:	8200
IV 22–40	11–18	V. 80	20800	9700	6500
				Average:	8150
		Mean:	24000	9350	6650
				Average:	8000 ± 17%

the maxima in the center and the minima in the periphery becoming greater in spite of a distribution according to the rules of good homogeneity.

Empirical dosage in interstitial cancer therapy expressed in r-equivalents (*Table III*).

The shortening of the time of application or wider spacing of radium in the center of large volumes shows up in the empirically developed dosage in interstitial therapy of cancers in the decreasing number of milligram-hours per cubic centimeter of treated volume.

Empirically the total dose was kept 20 per cent lower with the 2 mg. needles, though as a rule smaller volumes were treated with them than with the longer 3.3 mg. needles. The explanation is again the greater inhomogeneity of their radiation. In interstitial cancer therapy with the 2 mg. needles the minimum dosage is about 6,650, the average about 8,000 and the dose at the needle surfaces about 24,000 r-equivalents, while with the 3.3 mg. needles the minimum dosage is about 9,600, the average about 10,500 and the dose at the needle surfaces only about 17,000 r-equivalents. For the combined use of both needle types medium values are to be calculated.

Table IV

Comparison of calculated dosage and direct measurements

	Calculated	Measured
Distribution II.A		
Maxima 2 mm. dist.	135 r	121 r
Minima	109 r	97 r
Average:	122 r per h ±11%	109 r per h ±11%
Distribution II.B, III		
	Calculated	Measured
Average:	91 r per h ±20%	88 r per h ±25%

If a rough rule is established that in interstitial cancer therapy a dosage of about 1 mc-destroyed or 133 mg-hr. per cc. should be applied, it only very generally determines the tolerance of small volumes of tissue, not taking into account differences in the time factor. With the relatively high linear activities of 2 and 1.33 mg. per cm. we have to make short applications of only three to six days' duration and to decrease the dosage of 1 mc-destroyed per cc. already in a volume of only 10 cc. to about two-thirds mc-destroyed or 80 mg-hr. per cc. in volumes of 40–50 cc.

If the empirical dosage is calculated in r-equivalents after Tables I and II, it turns out to be remarkably constant for the different sizes of volume. The variation is only ±10 per cent of the mean in the case of the 3.3 mg. needles with their more homogeneous distribution of radiation and ±17 per cent in the case of the 2 mg. needles.

Empirically no regard was paid to the variation of the time factor between 1:1.5.

Ad II and III. *Comparison of calculated dosage and direct measurement* (*Table IV*).

The constancy of dosage expression in r-equivalents calculated for the empirical dosage in milligram-hours appeared almost too great to be correct and caused the direct dosage measurements of series II. In the result the measured value was 10 per cent lower than the calculated value.

Other control figures were available from measurements already made and published in 1932. By these measurements the intratumoral dosage in interstitial therapy of cancer of the tongue had been checked and for the first time been expressed in r-equivalents. The result of these three series of measurements differs only 3 per cent from the value calculated later. It is again a

little lower than the calculated value. The measured percentage of variation is a little higher, probably because the localization of the minima was not yet very exactly defined in the early measurements. The results of the three series of measurements differed in less than 5 per cent among themselves.

In our experiments there was agreement between dosage measurement and calculation. In the clinical work the reactions and results of therapy dosage planned after Table II were of great uniformity. That applies not only for interstitial therapy of cancer, in which differences between lethal and superlethal dosage might not always be perceptible, but especially for the reactions after interstitial therapy of benign lesions, hemangiomas and keloids, for which the approved dosage of surface therapy was planned after Table II.

Single test comparisons with absolute r-values obtained from Laurence's formulas and curves for calculation of interstitial radium dosage proved the r-equivalent values of our radium doses to be about 30 per cent lower.

Figure 5 shows a comparison with the r-values of Paterson and Parker. The three curves at the left show the number of milligram-hours necessary for 1,000 r minimum dosage for volumes up to 50 cc. In this comparison the curve from Paterson and Parker is about the mean of the curves for our needle types (a) and (b), (a) giving higher, (b) lower values in r-equivalents. The coincidence of the mean curve with that of Paterson and Parker might give the impression of good agreement of dosage after the two methods. But for cancer therapy our dosage is about 20–30 per cent higher expressed in milligram-hours and in r-equivalents. This difference might be real. In this case our dosage, given in a relatively short time, should after the available experience surpass the limit of tolerance. But actually ten years' experience does not indicate this. The difference in the number of milligram-hours might be based on different estimation of the treated volume and the difference in the expression in roentgen and roentgen-equivalents in differences of their absolute values. Contrary to the comparison with the values from Laurence the r-equivalents of our doses would in this case be about 20–30 per cent higher than the calculated roentgens of Paterson and Parker.

Such discrepancies emphasize the necessity of adequate measurement controls of

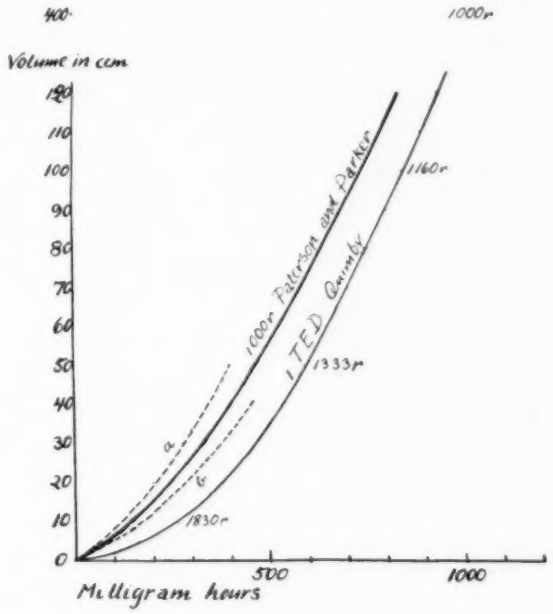

Fig. 5

calculated dosage in roentgens for extensive radium application.

If Quimby's curve showing the milligram-hours necessary for 1 T.E.D. in different volumes of tissue is calibrated in roentgens by the curve of Paterson and Parker, the dose expression for 1 T.E.D. in r varies with the volume from 1,800 r for 10 cc. to 1,000 r for 400 cc. Or the other way round, Paterson's total minimum dosage in interstitial cancer therapy corresponds to 3.2–6 T.E.D., the dosage expression in T.E.D. increasing with the volume, the time factor remaining constant and being of the same order for Quimby and Paterson.

The use of the demonstrated dosage rate table in r-equivalents can be recommended

for the application of needle types of the same active length. For the same active lengths but different linear activities the dosage rate in r-equivalents can easily be calculated from the relation of the linear activities. Corrections for different filtration must be applied. Thicker filters will hardly be used in interstitial therapy. With 0.3 mm. gold or platinum filtration the dosage rate increases about 5 per cent for the minimum rate in tissue of Tables II and III. In the case of different active length between 1 and 1.5 cm. an approximate estimation of the interstitial dosage in r-equivalents may be calculated from the mean value of our two needle types and the relation of the milligram radium content per centimeter estimated activity. The routine work with the different needle types here available has given adequate reactions and results with the dosage planned in this way.

The knowledge of radium dosage in roentgens or roentgen-equivalents is desirable not only for research work but for more exact clinical studies of the therapeutic effect and the judgment of tissue tolerance in the large number of cases which are sent for radium therapy after previous irradiations or for combined radium and roentgen therapy.

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DISCUSSION OF PAPERS OF DRS. COMPTON AND HAMANN

Dr. K. Wilhelm Stenstrom, Minneapolis, Minn. Biophysics was once the stepchild of the medical sciences and it is not until recently that it has received a better position. It is, of course, a rather exacting field for doctors to digest; nevertheless, I trust that you will remember for a long time the lecture that Dr. Compton has given. It is the best you can get both as far as content and recitation are concerned.

It is true that the exchange of energy inside the living cell is complicated and the changes which take place have to be studied biologically but we must admit that any explanation of what happens must be in agreement with the physical facts. When we play around with theories and hypothesis in biology or medicine, we often run up against seemingly contradictory experimental results. It does not worry us very much because so many uncontrolled factors come into the experiments; the contradictions may disappear by adding some new assumptions concerning these factors.

The physical experiments are usually better controlled, can be critically analyzed, and reliable conclusions can, as a rule, be obtained. It is therefore important that the theories we apply to our biological problem do not contradict the physical facts, and considerable help can thus be obtained from the physical factors. Unfortunately, that has often been neglected in the past, but this neglect is rapidly disappearing.

Dr. Compton called attention to the fact that the penetrating rays behave a little differently in that the ionization is much more concentrated when neutrons are used than when roentgen rays are used. It is difficult to state whether this should produce any biological difference; therefore, careful experiments must be carried out, and when it comes to studying the effect it is no doubt best to compare the neutrons and the roentgen rays, but of course we can also study the effect biologically on very small objects and then I believe that it is better

to compare the effects of penetrating alpha rays and electrons and such experiments have been started at several places. It may be that those experiments will give a more clear-cut picture than if you compare the effects from neutrons with those roentgen rays.

In fact there are two differences between the neutrons and the roentgen rays and one is that the neutrons act on the hydrogen atoms producing proton rays. The other factor is that the ions are much closer together in the paths of the protons than of the electrons. As far as I know, there is no difference in the ionization between those two types of rays except that the ions are closer together with the protons.

The main effect of the neutrons consists in the production of proton radiation. The more hydrogen present, the more effective the neutrons, but even in pure hydrogen it is only one atom here and one there that is hit and the distance between the individual proton rays thus produced is relatively large. Tissues containing more hydrogen should be particularly affected but it is doubtful that a specific action is produced in this manner as it is improbable that hydrogen is present in greater concentration in some cells than in others.

Dr. Hamann has presented an interesting paper, which is of particular value as a series of new measurements have been carried out. It is undoubtedly desirable that all radium therapists become accustomed to expressing the tissue dosage in equivalent roentgens. The reasons for this have been so well emphasized that it seems unnecessary to review them again. Some reservation must be made concerning the biological effect, which may not be the same for the same number of roentgens produced with rays of different hardness; thus the threshold erythema requires a different number of roentgens for roentgen rays of half-value layer 1 mm. and 0.1 mm. copper, and a still larger number of γ-ray roentgens. There seems to be satisfactory agreement that a point source of 1 mg. of radium filtered with 0.5 mm. platinum in one hour gives a dose of 8.3 or 8.4 r at 1 cm. distance. At the meeting of the American Radium Society we presented a report where we had adopted 8.3. Even though the difference is small, it would be preferable if we all agreed upon the same value, and I hope this can be done soon. With this value fixed the dosage in roentgens can be calculated at different distances from different types of applicators, as was pointed out by Dr. Hamann and as particularly demonstrated by Paterson and Parker. Such calculations ought to be checked by measurements as far as possible.

The greatest difficulty in estimation of the dose, either from previous measurements or calculations, arises from the distribution of the applicators (needles or implants) in the tissues, which may not be exactly what it is believed to be. It seems to me that the applicators should as far as possible be distributed at the periphery in spherical shells. This was also pointed out by Mayneord. The dose ought to increase approximately as the square of the diameter of the mass irradiated and not in proportion to the volume. I think that to say that we are irradiating so many cubic centimeters is not satisfactory. We should rather refer to the square of the diameter. The statement holds true, of course, only if the dosage rate remains the same, so that if the diameter is doubled the amount of radon or radium used is assumed to be four times as great. If the dose rate is changed, the problem becomes much more complicated, and it is doubtful that anybody can predict the correlation between the effect on the tissues and the dose rate at the present time. The variation with rate can be determined only by biological studies on selected types of tissues.

It is to be expected that measurements with certain types of applicators should give values which differ somewhat from the calculations. The measurements discussed here seem to agree reasonably well with the calculations of Paterson and Parker, and indicate that such calculations are satisfactory as approximations. We cannot expect complete agreement because the calculations are made with certain assumptions as far as the applicators are concerned, and the applicators used in these experiments were not exactly like those for which the calculations were made.

There is, of course, some question about the accuracy of the photographic method. The angle under which the rays strike the film and the time of exposure undoubtedly influence the blackening, and there may be a variable amount of radiation which has selective action on the photographic film. It is not probable that these factors influence the blackening to a great extent and it is interesting to see that repeated experiments give as good agreement as Dr. Hamann has pointed out. The measurements are a welcome addition to our knowledge of the

distribution of radiation and it is hoped that more papers of this type will be presented in the future.

Dr. Compton (closing). I should like to emphasize just one point that Dr. Stenstrom brought forward, that it is possible to get some of the contrasting effects between the concentrated ionization and more diffused ionization by experiments with alpha rays as compared with roentgen rays if one deals, as Dr. Stenstrom intimated, with very small organisms. One cannot, unfortunately, do those experiments with large organisms because the alpha rays penetrate only to a tenth of a millimeter or so, and so organisms of that order of dimensions have to be used for such experiments.

I might emphasize, then, that so far as future developments in different types of radiation are concerned, the best hope that we have of getting anything different from what we now have with roentgen rays is in connection with the neutrons unless some as yet unseen developments arise. Nevertheless there are certainly many things to be learned in the changing of the mode of application of roentgen rays, and I should like to urge the importance of investigating further that particular aspect of the subject.

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EDITORIALS

PREPYLORIC ULCER AND CARCINOMA

SAMPSON and Sosman,[1] in a recent paper on prepyloric ulcer and carcinoma, say that little has been written concerning the comparative frequency of benign ulcer and carcinoma of the prepyloric region, though considerable discussion has taken place concerning this occurrence. They quote Hampton as saying that benign ulceration in this region of the stomach is of such infrequent occurrence that all prepyloric ulcers should be considered malignant until proved otherwise. In Hampton's review of the literature and analysis of the cases which he observed at the Massachusetts General Hospital, he found the proportion of carcinomas to benign ulcers in the ratio of twelve to one. Singleton, on the other hand, in a study of the cases at the Toronto General Hospital found that benign prepyloric ulcers were twice as frequent as malignant ulcers.

In an attempt to harmonize such divergent opinions, Sampson and Sosman mention several difficulties which are encountered, and they place first among these the establishment of what is meant by prepyloric. They find that this term is rather loosely used not only by roentgenologists but also by surgeons and pathologists, some calling all lesions distal to the incisura angularis as in the prepyloric area and others restricting the meaning to the distal centimeter or so immediately adjacent to the pyloric region. Hampton, in his study, has limited the prepyloric region to exactly 1 inch proximal to and excluding the ring, and he has specified that for an ulcer to be truly prepyloric its center must be not more than 2.5 cm. from the ring.

In an attempt to evaluate the importance of Hampton's observation, Sampson and Sosman reviewed the 545 cases admitted to the Peter Bent Brigham Hospital. This group represented those cases of gastric ulcer and gastric carcinoma which were subjected to operation or autopsy during the twenty-five year period from the opening of the Hospital in 1913 to the end of 1937. In classifying the lesions as prepyloric they adhered strictly to Hampton's definition.

As a result of the analysis of this group of cases, they found that chronic ulcers in the prepyloric niche are cancerous in 75 per cent. These small prepyloric ulcers defy diagnosis by all means except histological examination and occasionally the pathologists have erred in some cases because an insufficient number of sections were cut and examined. Sampson and Sosman, in agreement with others, suggest that prepyloric ulcers which do not disappear entirely in a few weeks should be treated by radical resection and even in those cases where there has been an apparent disappearance of the prepyloric ulcer under medication the patient should be re-examined periodically.

In a recent report by Payne[2] on cancer of the stomach, attention is called to the roentgen investigations which provided a clue to the frequency of growth at the various sites in the stomach in 309 cases. Of these, 63.8 per cent, or approximately two-thirds, involved the pyloric region. Since the prepyloric region is such a favorite site for the occurrence of carcinoma of the stomach and in the earliest manifestation offers such hope of cure, the importance of ulcerative lesions in this region and the probability of their being of a cancerous nature should be constantly kept in mind.

[1] Sampson, D. A., and Sosman, M. C. Prepyloric ulcer and carcinoma. Am. J. Roentgenol. & Rad. Therapy, 1939, *42*, 797–810.

[2] Payne, R. T. Cancer of the stomach as a surgical problem. *Brit. J. Surg.*, April, 1940, *27*, 740–759.

LATERAL PYELOGRAPHY

A WELL established routine method in the examination of the patient enables one to arrive at a correct diagnosis. However, a too slavish attitude toward routine may prevent arrival at a correct diagnosis, as not infrequently another point of view or study will bring out a wealth of detail and information not thought of before.

Our attention has happily been called to this by a recent report by Shiflett and Keith[1] on their pyelographic studies. They emphasize the inportance of a lateral pyelogram as being helpful in clarifying certain obscure lesions. They do not recommend this examination as a routine procedure but only in certain definitely indicated cases. The technique is simple and it entails the use of no unusual equipment. The patient should be in an exact lateral position with of course the suspected pathologic kidney next to the film. With the patient in this direct lateral position, the ureter, pelvis and calyces of the suspected kidney are filled with the opaque medium and sufficient exposure given to bring out the detail of these structures. Of course in larger individuals there should be an increase in the concentration of the pyelographic medium.

The best results are obtained by a retrograde technique in the study in the lateral plane, but in many cases, where there is considerable stasis, studies in the lateral position during intravenous urography are of great benefit. Not only may the lateral pyelogram help to establish the type and degree of rotation of the kidney but information is given as to the displacement of the kidney or the ureter particularly in renal neoplasms and cysts, perinephric abscesses and primary retroperitoneal tumors as well as retroperitoneal infections and tumors arising from organs adjacent to the kidney and certain other abnormalities of kidney and ureter such as might be encountered in the investigation of the urinary tract.

Menville[2] had previously called attention to the importance of the lateral study, particularly in perinephric abscesses, and to the fact that the accuracy of the lateral pyelogram is dependent on the patient's lying perpendicular to the film. In the lateral pyelograms in the presence of a perinephric abscess there was a uniform anterior arch-like displacement of the kidney and ureter on the affected side.

Since the retroperitoneal space is potential any increase in solid or fluid medium from inflammation manifests itself by extension along the natural planes of tissue cleavage and by displacement of organs in the direction of least resistance which is usually forward and downward. The amount of displacement, of course, depends on the extent of the infiltration and the degree of suppuration.

Shiflett and Keith conclude that when careful studies are made in the direct lateral plane and these studies correlated with the clinical course of the case perinephric abscesses should be diagnosed relatively easily, which is not too frequently done. This simple method of examination would decrease the number of explorations for acute abdominal conditions which may be secondary to peritoneal irritation from the perinephric abscess which goes unrecognized. From the report of Shiflett and Keith there can be little doubt that the lateral pyelogram offers considerable information which may not be obtained in the usual routine examinations. Since the method is so simple, it should be used frequently to aid in differential diagnosis between intra-abdominal and retroperitoneal tumors and in the differentiation of retroperitoneal lesions themselves. Lateral pyelography should become almost as routine in the study of the ureters and kidneys as is the lateral study of the chest in pulmonary and cardiac conditions.

[1] Shiflett, E. L., and Keith, D. Y. Lateral pyelography. Am. J. Roentgenol. & Rad. Therapy, May, 1940, *43*, 664–672.

[2] Menville, J. G. The lateral pyelogram as a diagnostic aid in perinephric abscess. *J. Am. M. Ass.*, 1938, *111*, 231–233.

WALTER WENDELL FRAY
1892-1940

DR. WALTER WENDELL FRAY, aged forty-seven, Assistant Professor of Radiology at the University of Rochester, School of Medicine and Dentistry, died July 10, 1940, of chronic leukemia after an illness of five years' duration.

Dr. Fray received his B.S. and M.S. from Syracuse University in 1916 and 1917 respectively, and his M.D. from Harvard Medical School in 1922. He was House Physician in Medicine at the Massachusetts General Hospital in 1922, and Resident at the Willard Parker Hospital in 1924. In 1925, Dr. Fray came to the Strong Memorial Hospital as an Associate Resident in Medicine (Radiology) and has been associated with the radiology group ever since, becoming Assistant Professor of Medicine (Radiology) and Assistant Radiologist to the Strong Memorial Hospital in 1930. He had charge of the diagnostic roentgenological service of the hospital until his illness restricted his activities. With a change in organization of the department, he became Assistant Professor of Radiology in 1939.

Dr. Fray was made a Fellow in the American College of Radiology in 1937, a diplomate of the American Board of Radiology in 1934, and was a member of the American Roentgen Ray Society, American Medical Society, New York State and Monroe County Medical Societies, Rochester Roentgen Ray Society, Rochester Academy of Medicine.

Dr. Fray was a shrewd diagnostician and

an excellent teacher. His research interests were divided among several diagnostic fields, his work on coarctation of the aorta, cardiac mensuration, and pineal localization being best known. He had been keenly interested in the silicosis problem, and had recently been working with experimental lesions produced in rabbits by dust particles.

Dr. Fray's chief hobbies were photography and gardening, the latter being a consuming passion during the last few years.

By his death, our group will miss not only a stimulating thinker and a capable radiologist, but also a fine man and a delightful friend.

Stafford L. Warren

SOCIETY PROCEEDINGS, CORRESPONDENCE AND NEWS ITEMS

Items for this section solicited promptly after the events to which they refer.

MEETINGS OF ROENTGEN SOCIETIES*

United States of America

American Roentgen Ray Society
Secretary, Dr. C. B. Peirce, Royal Victoria Hospital, Montreal, Canada. Annual Meeting: Hotel Statler, Boston, Mass., Oct. 1–4, 1940.

American College of Radiology
Secretary, Mac F. Cahal, 540 N. Michigan Ave., Chicago, Ill. Next annual meeting: 1941, to be announced.

Section on Radiology, American Medical Association
Secretary, Dr. J. T. Murphy, 421 Michigan St., Toledo, Ohio. Annual meeting: 1941, to be announced.

Radiological Society of North America
Secretary, Dr. D. S. Childs, 607 Medical Arts Bldg., Syracuse, N. Y. Annual meeting: Cleveland, Ohio, Dec. 2–6, 1940.

Radiological Section, Baltimore Medical Society
Secretary, Dr. Walter L. Kilby, Baltimore. Meets third Tuesday each month, September to May.

Radiological Section, Connecticut Medical Society
Secretary, Dr. Max Climan, 242 Trumbull St., Hartford, Conn. Meets twice annually in May and September.

Section on Radiology, Illinois State Medical Society
Secretary, Dr. H. W. Ackemann, 321 W. State St., Rockford, Ill.

Radiological Section, Los Angeles Co. Med. Soc.
Secretary, Dr. Wilbur Bailey, 2007 Wilshire Blvd., Los Angeles, Calif. Meets on second Wednesday of each month at County Society Building.

Radiological Section, Southern Medical Association
Secretary, Dr. Roy G. Giles, Temple, Texas.

Brooklyn Roentgen Ray Society
Secretary, Dr. L. J. Taormina, 1093 Gates Ave., Brooklyn, N. Y. Meets monthly on first Tuesday, October to April.

Buffalo Radiological Society
Secretary-Treasurer, Dr. Joseph S. Gian-Francheschi, 610 Niagara St., Buffalo, N. Y. Meets second Monday of each month except during summer months, place of meeting selected by the host.

Chicago Roentgen Society
Secretary, Dr. C. J. Challenger, 3117 Logan Blvd. Meets second Thursday of each month October to April inclusive at the Palmer House.

Cincinnati Radiological Society
Secretary, Dr. J. E. McCarthy, 707 Race St., Cincinnati, Ohio. Meets third Tuesday of each month, October to May, inclusive.

Cleveland Radiological Society
Secretary, Dr. H. A. Mahrer, 10515 Carnegie Ave. Meets at 6:30 P.M. at Mid-Day Club rooms on fourth Monday each month, October to April, inclusive.

Denver Radiological Club
Secretary, Dr. P. R. Weeks, 520 Republic Bldg., Denver, Colo. Meets third Friday of each month.

Detroit Roentgen Ray and Radium Society
Secretary, Dr. E. R. Witwer, Harper Hospital. Meets monthly on first Thursday from October to May, at Wayne County Medical Society Building.

Florida State Radiological Society
Secretary, Dr. J. N. Moore, 210 Professional Bldg., Ocala, Florida. Meetings in May and November.

Georgia Radiological Society
Secretary, Dr. R. C. Pendergrass, Prather Clinic Bldg., Americus, Ga. Meets in November and at annual meeting of Medical Association of Georgia in the spring.

Illinois Radiological Society
Secretary, Dr. Wm. DeHollander, St. John's Hospital, Springfield, Ill. Meetings held quarterly, on the fourth Sunday of the month.

Indiana Roentgen Society
Secretary, Dr. C. C. Taylor, 23 E. Ohio St., Indianapolis, Ind. Meeting held the second Sunday in May annually.

Kentucky Radiological Society
Secretary, Dr. J. C. Bell, 402 Heyburn Bldg., Louisville. Meets annually in Louisville on third Sunday afternoon in April.

Long Island Radiological Society
Secretary, Dr. Marcus Wiener, 1430-48th St., Brooklyn, N. Y. Meets Kings County Med. Soc. Bldg. monthly on fourth Thursday, October to May, 8:30 P.M.

Michigan Association of Roentgenologists
Secretary, Dr. J. E. Lofstrom, 1536 David Whitney Bldg., Detroit. Three meetings a year, Fall, Winter, Spring.

Milwaukee Roentgen Ray Society
Secretary, Dr. I. I. Cowan, Mt. Sinai Hospital, Milwaukee, Wis. Meets monthly on first Friday at University Club.

Minnesota Radiological Society
Secretary, Dr. J. P. Medelman, 572 Lowry Medical Arts Bldg., St. Paul.

Nebraska Radiological Society
Secretary, Dr. D. A. Dowell, Medical Arts Bldg., Omaha, Nebr. Meets third Wednesday of each month, at 6 P.M. at either Omaha or Lincoln.

New England Roentgen Ray Society
Secretary, Dr. A. O. Hampton, Massachusetts General Hospital, Boston, Mass. Meets monthly on third Friday, Boston Medical Library.

Radiological Society of New Jersey
Secretary, Dr. W. J. Marquis, 198 Clinton Ave., Newark. Meets annually at time and place of State Medical Society. Mid-year meetings at place chosen by president.

New York Roentgen Society
Secretary, Dr. R. D. Duckworth, 170 Maple Ave., White Plains, N. Y. Meets monthly on third Monday, New York Academy of Medicine, at 8:00 P.M.

North Carolina Roentgen Ray Society
Secretary, Dr. Major Fleming, Rocky Mount, N. C. Annual meeting at time and place of State Medical Society. Mid-year scientific meeting at place designated.

Central New York Roentgen Ray Society
Secretary, Dr. C. F. Potter, 820 S. Crouse Ave., Syracuse. Three meetings a year. January, May, November.

Ohio Radiological Society
Secretary, Dr. J. E. McCarthy, 707 Race St., Cincinnati. Meets at time and place of annual meeting of Ohio State Medical Association.

Pacific Roentgen Society
Secretary, Dr. L. H. Garland, 450 Sutter St., San Francisco, Calif. Meets annually, during meeting of California Medical Association.

Pennsylvania Radiological Society
Secretary, Dr. L. E. Wurster, 416 Pine St., Williamsport Pa. Meets annually.

Philadelphia Roentgen Ray Society
Secretary, Dr. B. R. Young, Temple University Hospital. Meeting first Thursday of each month from October to May inclusive, at 8:15 P.M., in Thompson Hall, College of Physicians, 19 S. 22d St.

Pittsburgh Roentgen Society
Secretary, Dr. W. H. Jacox, 4800 Friendship Ave. Meetings held second Wednesday each month, 4:30 P.M., October to June at various hospitals.

Rochester Roentgen Ray Society, Rochester, N. Y.
Secretary, Dr. S. C. Davidson, 277 Alexander St. Meets on second Thursday from October to May, inclusive, 8 P.M., Rochester Academy of Medicine Building.

St. Louis Society of Radiologists
Secretary, Dr. W. K. Mueller, University Club Bldg. Meets fourth Wednesday of October, January, March and May, at a place designated by the president.

San Francisco Radiological Society
Secretary, Dr. H. A. Hill, 450 Sutter St., San Francisco. Meets monthly on third Thursday at 7:45 P.M., first six months at Toland Hall, second at Lane Hall.

* Secretaries of Societies not here listed are requested to send the necessary information to the Editor.

South Carolina X-Ray Society
Secretary, Dr. T. A. Pitts, Baptist Hospital, Columbia, S. C. Meets in Charleston on first Thursday in November, also at the time and place of South Carolina State Medical Association.

Tennessee Radiological Society
Secretary, Dr. F. B. Bogart, 311 Medical Arts Bldg Chattanooga, Tenn. Meets annually at the time and place of the Tennessee State Medical Association.

Texas Radiological Society
Secretary, Dr. L. W. Baird, Scott and White Hospital, Temple, Texas. Next annual meeting, January 18, 1941, Sherman, Texas.

University of Michigan Department of Roentgenology Staff Meeting
Meets each Monday evening from September to June, at 7 P.M. at University Hospital.

University of Wisconsin Radiological Conference
Secretary, Dr. E. A. Pohle, 1300 University Ave., Madison, Wis. Meets every Thursday from 4:00–5:00 P.M., Room 301, Service Memorial Institute.

Virginia Radiological Society
Secretary, Dr. V. W. Archer, University Hospital, University, Va. Meets annually in October.

Washington State Radiological Society
Secretary, Dr. K. J. Holtz, American Bank Bldg., Seattle. Meets fourth Monday of each month at the College Club, Seattle.

Cuba

Sociedad Cubana de Radiologica y Fisioterapia
Secretary, Dr. Francisco Padron, Enrique, Villuendas 64, Havana, Cuba. Meets monthly in Havana.

British Empire

British Institute of Radiology Incorporated with the Röntgen Society
Meets monthly on third Thursday from November to June inclusive, at 8:15 P.M., 32 Welbeck St., London.

Section of Radiology of the Royal Society of Medicine (Confined to Medical Members)
Meets on the third Friday of each month during the winter at 8:15 P.M. at the Royal Society of Medicine, 1, Wimpole St., London, W. 1.

Faculty of Radiologists
Secretary, Dr. Barbara M. Key, 32 Welbeck St., London, W. 1, England.

Section of Radiology and Medical Electricity, Australasian Medical Congress
Secretary, Dr. H. M. Cutler, 139 Macquarie St., Sydney, New South Wales.

Radiological Section of the Victorian Branch of the British Medical Association
Secretary, Dr. Keith Hallam, St. George's Hospital, K.E.W., Melbourne, E. 4, Victoria, Australia. Meets monthly from March to November inclusive for scientific discussion.

Canadian Association of Radiologists
Secretary, Dr. A. C. Singleton, Medical Arts Bldg., Toronto, 5, Ontario.

Section of Radiology, Canadian Medical Association
Secretary, Dr. C. M. Jones, Inglis St., Ext., Halifax, N. S.

Radiological Section, New Zealand British Medical Association
Secretary, Dr. Colin Anderson, Invercargill, New Zealand. Meets annually.

Continental Europe

Belgian Society of Roentgenology
Secretary, Dr. J. Boine, Avenue des Alliés, 134, Louvain (Belgium). Meets monthly on second Sunday at d'Egmonds Palace, Brussels, except in the summertime.

Sociedad Espanola de Radiologia y Electrologia
Secretary, Dr. J. Martin-Crespo, Fuencarral, 7. Madrid, Spain. Meets monthly in Madrid.

Société de Radiologie Médicale de France
Meets monthly on second Tuesday, except during months of August and September, 12 Rue de Seine, Paris.

Société Suisse de Radiologie (Schweizerische Röntgen-Gesellschaft)
Secretary for French language, Dr. A. Grosjean La Chaux de Fonds.
Secretary for German language, Dr. Scheurer, Molzgasse, Biel. Meets annually in different cities.

Société Francaise d'Electrothérapie et de Radiologie Médicale
Meets monthly on fourth Tuesday, except during months of August and September, 12 Rue de Seine, Paris.

Association of German Roentgenologists and Radiologists in Czecho-Slovakia
Secretary, Dr. Walter Altschul, German University, Prague, II.52.

Deutsche Röntgen-Gesellschaft (Gesellschaft für Röntgenkunde und Strahlenforschung)
Meets annually in April, alternating one year in Berlin, one year in some other German city. Meets in addition every two years with the Gesellschaft deutscher Naturforscher und Aertze.
Permanent Secretary, Professor Dr. Haenisch, Klopstockstrasse 10, Hamburg, Germany.

Süd- und Westdeutsche Röntgengesellschaft
Meets annually in different cities.

Nord- und Ostdeutsche Röntgengesellschaft
Meets annually in different cities.

Dutch Society of Electrology and Roentgenology
Holds two meetings a year in Amsterdam, one in the spring, and one in the fall.

Societa Italiana Radiologia Medica
Secretary, M. Ponzio, University of Turin, Prof. Turin.

Societatea Romana de Radiologie si Electrologie
Secretary, Dr. Oscar Meller, Str. Banul Mărăcine, 30, S. I., Bucuresti, Roumania. Meets second Monday in every month with the exception of July and August.

All-Russian Roentgen Ray Association, Leningrad, USSR in the State Institute of Roentgenology and Radiology, 6 Roentgen St.
Secretaries, Drs. S. A. Reinberg and S. G. Simonson. Meets annually.

Leningrad Roentgen Ray Society
Secretaries, Drs. S. G. Simonson and G. A. Gusterin. Meets monthly, first Monday at 8 o'clock State Institute of Roentgenology and Radiology, Leningrad.

Moscow Roentgen Ray Society
Secretaries, Drs. L. L. Holst, A. W. Ssamygin and S. T. Konobejevsky. Meets monthly on first Monday at 8 o'clock.

Polish Society of Radiology
Secretary, Dr. Jan Kochanowski, 45 Gornoslazka St., Warsaw. Meets annually.

Warsaw Section, Polish Society of Radiology
Secretary, Dr. B. Krynski, 11 Zielna St. Meets once a month except in the summertime.

Scandinavian Roentgen Societies
The Scandinavian roentgen societies have formed a joint association called the Northern Association for Medical Radiology, meeting every second year in the different countries belonging to the Association. Each of the following societies, with exception of the Denmark Society, meets every second month except in the summertime.

Society of Medical Radiology in Sweden
Meets in Stockholm.

Society of Medical Radiology in Norway
Meets in Oslo.

Society of Medical Radiology in Denmark
Secretary, Dr. G. Biering, Copenhagen. Meets the second Wednesday of each month from October to July in Copenhagen, at 8'oclock in the State Institute of Roentgenology.

Society of Medical Radiology in Finland
Meets in Helsingfors.

Vienna Roentgen Society
Meets first Wednesday of each month, at 6:30 P.M. at Zentral-Röntgen Institut des allgemeinen Krankenhauses Alserstrasse 4.

Orient

Japan X-Ray Association
c/o Orthopedic Surgery, Tokyo Imperial University. Meets annually in April.

Kinki Roentgen-Abend Society
Director, Dr. Prof. Taiga Saito, Ogawaoike Tyoto Japan. Meets bi-monthly on third Sunday.

BULLETIN OF THE INTER-SOCIETY COMMITTEE FOR RADIOLOGY

THE PROFESSIONAL BUREAU OF THE COLLEGE

This is a progress report. It covers the period between the February, 1940, meeting of the Board of Chancellors, American College of Radiology, in which it was decided to expand the activities of the Professional Bureau, and the June, 1940, meeting. A preliminary report appeared in the April issue of this Journal.

The expansion as outlined in the previous report and which was authorized by the Board of Chancellors has been completed. Printed forms including all biographical data as to education and training of applicants have been printed and distributed to all applicants and to the department heads of the 88 approved radiological training centers. In addition, forms have been printed for the use of institutions or individuals seeking a radiologist. On these forms, essential data are recorded showing financial arrangement, type of practice, equipment, whether or not the institution has had a radiologist.

Publicity articles were prepared and submitted to the executive secretary for distribution to hospitals and medical periodicals or wherever he deemed it essential that publicity should be given to the Professional Bureau. At the present time, the Bureau has 73 applicants. These may be tabulated as follows: Protestant, 40; Jewish, 22; Catholic, 7; Mormon, 1; Quaker, 1; Diplomate of the American Board of Radiology, 21; not Diplomates, 52. Financial arrangement preferred: salary, 28; percentage, 22; rental, 6; salary and percentage, 14. Expected income:

$2,000.00	1
2,500.00	5
3,000.00	8
3,500.00	12
4,000.00	12
4,500.00	2
5,000.00	15
More than $5,000.00	6
Not stated	10

Locality preferred: South, 5; North, 2; Midwest, 12; East, 5; Pacific Coast, 10; Southwest, 5. Full-time 64; part-time, 5; private practice, 2; would open private office, 2; has had position: yes, 32; no, 41. Interested in vacancy: in 1940, 53; 1941, 12; 1942, 8.

Letters received from institutions seeking applicants seem to indicate a definite trend towards full-time radiology and a complete divorce from part-time radiology practice in those institutions seeking a radiologist. Some of them frankly state that the staff is not satisfied with the pure film-reading service and no consultation that they are receiving. Some state that it is poor from a financial standpoint and some feel that, as a matter of competition, they must have a full-time radiologist.

Referring to the March 30, 1940, hospital number of the *Journal of the American Medical Association*, we find that there has been an increase in the number of hospitals with approved radiological departments at the rate of one hundred per year. This also shows an increase in a five-year period of seven hundred physician radiologists in charge. This evidently means that the five hundred installed during the five-year period took on a radiologist and about two hundred had the department turned over to some physician in order that they might have a physician director.

In the classification of residencies and fellowships, it shows that 49 men were in training in radiology in 1927, 66 in 1934, 110 in 1937, and 245 in 1940. Under "departments of radiology," the study shows that departments in charge of physician radiologists have increased, from 1934 to 1940, from 3,563 to 4,249. It is therefore evident that, excluding a certain number of approved radiologists who are, for statistical purposes, carried as in charge or director of the department in these hospitals, there are many such departments in charge of men who are not Diplomates of the American Board of Radiology. In view of the fact that there are 245 men now in training who are potential jobseekers, it is quite evident that some of these men will have to be displaced in favor of full-time and well-trained young radiologists.

It will be noted that the largest number of applicants are willing to start on a salary basis. In a recent survey conducted by the Pennsylvania State Radiological Society, it was found that the average income of radiologists on straight salary was $4,200.00 per year, and of those on a commission basis, income average was $7,600.00 per year. It will also be noted that more than half of the applicants are expecting less than the minimum salary found in this survey.

Since expansion of the Bureau, upon receipt of an opening, all applicants and all department heads are notified. A letter has been written to each of the openings, asking them what response they have had to notices sent out by the Bureau. Some have replied that they have had as many as 20 replies from our applicants, and every letter has been enthusiastic about the service rendered by the Professional Bureau and the number of responses that they have had due to contacts we have been able to give them with men looking for locations.

There has been some misunderstanding among some of the men as to the functions of the Professional Bureau. A number of them have referred men seeking a residency in radiology to us. We have also had some requests for residents and have attempted to bring both parties together. This seems a better method than a blunt refusal in such cases.

At the present time, the liveliest interest shown by institutions seeking radiologists is from the state of West Virginia. This is evidently due to knowledge of the existence of the Bureau being disseminated among hospitals in that particular locality. It is obvious when one reads the advertisements of commercial bureaus that all men seeking positions and all institutions seeking radiologists have not appealed to the Bureau, although there are undoubtedly some duplications. This is no implication that we expect to monopolize the placing of radiologists, but is used only as an indication that our publicity has not been fully effective.

It is not the purpose of this report to burden you with statistics, but a project like the Professional Bureau yields statistical information that is of value from the economic side of the practice of radiology. An attempt was made to evaluate or predict revenue from radiologic work in certain localities. This was brought about by the information we received in which it was clearly shown that the amount of work done in a locality or in an institution had no relation to the number of admissions or to the population. In earlier figures, it seemed that one could estimate that the potential revenue for radiologic work should be about one dollar per year per person.

Unfortunately, it is impossible to obtain accurate information pertaining to the total gross charges for radiologic work in communities of representative size.

Gross income for radiologists, as revealed by the economic survey conducted by the Inter-Society Committee last year, showed that the income for radiology was below that for orthopedic surgery, surgery, or proctology. This survey also showed the highest income in the East South-Central region and the lowest in New England. The ratio of radiologists to population is highest in the East South-Central, 1:124,000. In New England it is 1:48,000. This shows a correlation between the average population per radiologist and the average gross income for radiologists. By dividing the population per radiologist by the gross income of radiologists, we get an average expenditure per person for radiology in the East South-Central region of 12 cents and in New England of 18 cents. Carrying these figures further with the figures compiled by group hospital and sickness insurance plans and their calculated days of illness and expenditure for medical services, we come to the conclusion that about 75 cents per capita will be the expenditure for radiology in a prosperous community, down to 50 cents or below in the impoverished areas.

It is also a significant fact from the information sent to us pertaining to openings and the salary that they offer that in those institutions where the salary range for

radiologists is around $2,500.00 a year, we will find that roentgen examinations have a ratio to the admissions of 1:2 plus, while in those institutions desiring a higher class man, the ratio will be 1+:1. From this, one arrives at the conclusion that the amount of radiologic work done in an institution is directly proportionate to the caliber of the radiologist, and obviously, a man's income is directly proportionate to his ability. I am of the opinion that sufficient evidence can be collected to bear out these suppositions (obtained from a small amount of material) that this information will be enlightening to those hospitals desiring to hire radiologists at a technician's salary. Further statistics along this line will be compiled as available information presents itself and we hope to incorporate such figures in a future report.

Mac F. Cahal
Executive Secretary

COMMITTEES ON LOCAL ARRANGEMENTS

Any one desiring information on any particular phase of the Forty-first Annual Meeting of the American Roentgen Ray Society to be held in Boston, October 1–4, 1940 may write to the general chairman or to the chairman of the particular section desired.

General Chairman: Dr. A. O. Hampton, Massachusetts General Hospital, Boston.

Scientific Sessions: Chairman—Joseph H. Marks, Deaconess Hospital, Boston; Harvey Morrison (by invitation), L. Alexander Vance (by invitation).

Scientific Exhibits: Chairman—A. O. Hampton, Massachusetts General Hospital, Boston; Philip H. Cook, Richard Dresser, Hugh F. Hare, George Levene, Joseph H. Marks, Clarence N. McPeak, Albert M. Moloney, Samuel A. Robins, Edward C. Vogt, Stanley A. Wilson.

Instruction Courses: Chairman—Hugh F. Hare, Lahey Clinic, Boston; Richard Dresser, A. S. MacMillan, Magnus Smedal (by invitation), John Trump (by invitation), George M. Wyatt (by invitation).

Technical Exhibits: Chairman—Charles W. Blackett, 35 Bay State Rd., Boston; Ariel W. George, Andrew E. O'Connell.

Registration and Hotel: Chairman—Max Ritvo, 485 Commonwealth Ave., Boston; Thomas R. Healy, John H. Lambert.

Banquet and Entertainment: Chairman—Robert G. Vance, 264 Beacon St., Boston; George W. Holmes, Kenneth K. Kinney, John Sproull, Langdon T. Thaxter.

Public Relations: Chairman—Frederick W. O'Brien, 465 Beacon St., Boston; Percy Brown, Ralph B. Leonard.

Transportation: Chairman—Albert M. Moloney, 47 Bay State Rd., Boston; Edwin N. Cleaves, Frank E. Wheatley.

Willis F. Manges Golf Tournament: Chairman—P. F. Butler, 35 Bay State Rd., Boston; Michael J. Cox, William J. Elliott (by invitation), Charles Whelan (by invitation).

Ladies Entertainment Committee: Chairman—Mrs. Merrill C. Sosman, 24 Lee Road, Chestnut Hill, Mass.; Mrs. P. F. Butler, Mrs. Richard Dresser, Mrs. A. O. Hampton, Mrs. Hugh F. Hare, Mrs. George W. Holmes, Mrs. Robert G. Vance.

A separate announcement will be found in this issue concerning the golf tournament. The Caldwell Lecture will be given Tuesday night by Dr. George W. Holmes, Clinical Professor of Roentgenology, Harvard Medical School. The annual banquet will be held on Thursday night, preceded by a reception for members and guests given by the New England Roentgen Ray Society. All meetings will be held at the Hotel Statler.

ANNUAL GOLF TOURNAMENT

The annual Golf Tournament at the meeting of the American Roentgen Ray Society in Boston will be held at the Commonwealth Country Club on Monday, September 30, 1940. The Manges Memorial Trophy will be awarded to the lowest net scorer, who will be given the Trophy for one year and a replica for his permanent possession. Many other prizes will also be offered. The course is available for play all day. Luncheon and dinner will be served at the Club and prizes will be awarded at the dinner. Non-playing members are welcome at the dinner and it is hoped that a large

number will be present. Members desiring to play should write to the Chairman of the Golf Committee, Dr. P. F. Butler, 35 Bay State Road, Boston, Massachusetts, enclosing their club or state handicap. Those wishing to attend the dinner only should also send in their names. A charge of $6.00 will cover golf fees and dinner. A desk will be set up in the Hotel Statler on Sunday and Monday for information and sale of golf tickets.

P. F. Butler, *Chairman*
Michael J. Cox
William J. Elliott (by invitation)
Charles Whelan (by invitation)

LADIES' PROGRAM

FORTY-FIRST ANNUAL MEETING, AMERICAN ROENTGEN RAY SOCIETY

Because October in New England is one of the loveliest months, the Ladies' Committee is anxious that wives and daughters of the members of the American Roentgen Ray Society come to Boston with them. The following program has been planned for the ladies while the men are attending the scientific meetings.

On Tuesday afternoon there will be a trip to the Isabella Stewart Gardner Museum where guests will meet informally before making a tour of the Museum with guides. During the visit, there will be an hour of music in the Tapestry Room followed by tea in the Dutch Room. This trip is limited to one hundred persons, with admission by card only.

The following day, Wednesday, will find busses and guides at the door of the hotel about eleven o'clock for a trip through Cambridge, Concord, Lexington, Sudbury and back through residential Newton, Brookline and Boston.

In Cambridge there will be a stop at The University Museum to see the famous glass flowers; in Concord and Lexington, stops at the home of Louisa M. Alcott, Old North Bridge, The Old Manse and Lexington Green; and finally, at Sudbury, for lunch at the Wayside Inn. This old tavern, made famous by Hawthorne and preserved by Mr. Henry Ford, is one of the most interesting places in the vicinity of Boston. There are many of the familiar treasures of Hawthorne's Tales as well as the schoolhouse where Mary and her little lamb went to school.

Because of the banquet and entertainment at night, Thursday will be given over to short city tours for which busses will be available at the hotel. These tours include Paul Revere's house, Old North Church, Bunker Hill, Faneuil Hall, Old Ironsides and many other places famous in our American history.

For those who have taken these trips, there will be opportunity to make new acquaintances or to renew old ones.

With a most cordial greeting awaiting each guest, it is hoped that many and prompt replies will follow the receipt of reservation cards. These cards will be mailed to each member early in September.

The Ladies' Committee

CONFERENCE ON APPLIED NUCLEAR PHYSICS

October 28 — November 2, 1940

A General Conference on Applied Nuclear Physics, sponsored by the American Institute of Physics in cooperation with the Massachusetts Institute of Technology, will be held during the week of October 28–November 2, 1940, at the Massachusetts Institute of Technology, Cambridge, Massachusetts. The rapidly increasing number of applications of methods and apparatus characteristic of nuclear physics in the fields of biology, radiology, chemistry, geology, and industrial physics has long emphasized the usefulness of a joint conference between physicists and their colleagues in other fields of science.

The purposes of the Conference are to bring together investigators who may be widely separated geographically, and to provide a forum for assembling and correlating present knowledge and difficulties, and for directing attention toward fundamental lines of research which should be the subject of future investigations.

The week's activities will be divided into separate sessions on applications to biology, chemistry, radiology, metallurgy, geology, and to general sessions relating to the production and use of radioactive and stable isotopes, and the protection of workers from radiation. An outline of the general program is given in the following table:

Conference on Applied Nuclear Physics

Digest of Program

Monday A.M., October 28, 1940 (two parallel sessions)
- *Geology I:* "Techniques and Standards in Terrestrial Radioactivity Measurements."
- *Metallurgy I:* "Tracer Studies of Metal Diffusion and Corrosion."

Monday P.M., October 28, 1940 (two parallel sessions)
- *Geology II:* "Geochemical Applications of Radioactivity."
- *Metallurgy II:* "Radiography with Gamma-Rays, X-Rays, and Neutrons."

Tuesday A.M., October 29, 1940 (three parallel sessions)
- *Geology III:* "Radioactive Methods of Geologic Age Determinations."
- *Chemistry I:* "Tracer Techniques in General Chemistry."
- *Radiology I:* "General Aspects of Cancer Therapy."

Tuesday P.M., October 29, 1940 (three parallel sessions)
- *Geology IV:* Geophysical Applications of Nuclear Physics."
- *Chemistry II:* "Tracer Techniques in Analytical Chemistry."
- *Radiology II:* "Radium and Roentgen Therapy."

Wednesday A.M., October 30, 1940
- *General I:* "Production of Radioactive and Stable Isotopes and of Penetrating Radiations."

Wednesday P.M., October 30, 1940
- *General II:* "Measurement of Radioactive and Stable Isotopes and of Penetrating Radiations."

Thursday A.M., October 31, 1940
- *General III:* "Protection of Workers from Biological Effects of Radiation."

Thursday P.M., October 31, 1940 (three parallel sessions)
- *Chemistry III:* "Synthesis of Organic Substances Containing Tracers."
- *Radiology III:* "Neutron and Artificial Radioactivity Therapy."
- *Biology I:* "Tracer Techniques in Biology."

Friday A.M., November 1, 1940 (two parallel sessions)
- *Radiology IV:* "Dosage Measurements."
- *Biology II:* "Tracer Studies of Plant and Animal Metabolism."

Friday P.M., November 1, 1940 (two parallel sessions)
- *Radiology V:* "Radiobiology."
- *Biology III:* "Tracer Studies" (continued).

Saturday A.M., November 2, 1940 (two parallel sessions)
- *Biology IV:* "Tracer Studies" (concluded).
- *General IV:* "Contributed Papers."

Committee in Charge of Program

Robley D. Evans, *Chairman*
Massachusetts Institute of Technology

Elmer Hutchisson, *Secretary*, University of Pittsburgh
Henry A. Barton, American Institute of Physics
Edw. U. Condon, Westinghouse Electric & Manufacturing Company
Lee A. DuBridge, University of Rochester
G. Failla, Memorial Hospital, New York
Clark Goodman, Massachusetts Institute of Technology
Ernest O. Lawrence, University of California
Harold C. Urey, Columbia University

The daily sessions will consist of short invited papers by leading investigators followed by vigorous and searching discussion by the conferees. Ample time will be allowed between and after regular sessions for personal and informal conferences. While the emphasis will be on the program of invited papers and the discussion of these, provision has also been made for a limited number of ten-minute contributed papers. Five one-hour evening sessions will be held, in each of which an outstanding investigator will summarize the status of the several fields which are joined together by the Conference. The evening lectures will be open to the general public.

Anyone who can actively participate in or profit by the Conference is eligible and cordially invited to become a member. Advance registration (no fee) will be required to permit suitable arrangements to be made. Those wishing to attend should register by letter as soon as possible and not later than October 1. Letters and inquiries should be addressed to Professor Robley D. Evans, General Chairman, Conference on Applied Nuclear Physics, Massachusetts Institute of Technology.

1940 GRADUATE FORTNIGHT OF THE NEW YORK ACADEMY OF MEDICINE

The 1940 Graduate Fortnight of The New York Academy of Medicine will be held from October 14 to 25, 1940.

The subject of this year's Fortnight is *Infections*. The purpose of the Fortnight is to make a complete study and authoritative presentation of a subject of outstanding importance in the practice of medicine and surgery.

The Fortnight will present a carefully integrated program which will include morning panel discussions, afternoon clinics and clinical demonstrations at many of the hospitals of New York City, evening addresses, and appropriate exhibits. The evening sessions at the Academy will be addressed by recognized authorities in their special fields, drawn from leading medical centers of the United States. The comprehensive exhibit will include books and roentgenograms; pathological and research material; and clinical and laboratory diagnostic and therapeutic methods. It is also planned to provide demonstrations of exhibits.

The subject of the Fortnight will include the following:

Experimental basis of chemotherapy in the treatment of bacterial infections
Clinical bacterial chemotherapy, results obtained and dangers encountered
A general consideration of bacterial infections
Recent advances in knowledge of streptococcal infections
Infections of mouth, pharynx and upper respiratory tract
Infections of middle ear and nasal sinuses
Infections of teeth and surrounding structures
Influenza
Pneumococcal infections
Bacterial meningitis
Infections of the urinary tract
Gonococcal infections in the male
Gonococcal infections in the female
Osteomyelitis and pyogenic infections of joints
Wound infections
Puerperal infections
Treatment of infections by methods other than chemotherapy
Virus infections
Acute poliomyelitis
Brucellosis—undulant fever
Rickettsial diseases
Lymphogranuloma venereum
Epidemic encephalitis
Other forms of encephalitis and choriomeningitis
Exanthematous diseases

The Academy provides this program for the fundamental purpose of medical education, consequently all members of the medical profession are eligible for registration.

A complete program and registration blank may be secured by addressing Dr. Mahlon Ashford, The New York Academy of Medicine, 2 East 103 Street New York City.

SUMMARY OF REPORT OF COMMISSION ON GRADUATE MEDICAL EDUCATION

Important developments in the hospital internship, the hospital residency and the postgraduate educational opportunities for physicians in practice were suggested by the Commission on Graduate Medical Education, whose final report was published on June 25, 1940. The Commission, which was organized by the Advisory Board for Medical Specialties on December 4, 1937, is now bringing to a close its three year study program. Its work has been financed by national foundations and interested professional organizations.

The internship, suggests the Commission, should be considered as a basic preparation for the practice of medicine. It should round out and give practical application to the medical school course and hence should be closely allied to undergraduate medical education. It should prepare young physicians adequately to begin general family practice and should provide them with the essential preparation necessary to undertake further study leading to the practice of a specialty. It should not attempt to

train men for the specialties directly, and therefore the intern should not be given training in the detailed techniques of the specialties.

To prepare the intern for general practice, he should have experience in internal medicine, pediatrics, obstetrics and gynecology, and surgical diagnosis, minor surgery and treatment of emergencies. Special attention in these fields should be given to preventive medicine and the care of chronic diseases, conditions of the aged and functional disturbances. The whole atmosphere should be educational in character and the intern should learn by example as well as precept.

The residency is defined by the Commission as a prolonged period of study in one of the special fields which can be properly classed as graduate education, whether an advanced degree is granted or not. The Commission warmly supports the recommendation of the specialty boards that adequate attention be given during the residency to the basic sciences as they relate to the various specialties. It suggests practical ways by which hospitals may provide this basic science training in their own laboratories or through arrangements with medical schools. The report suggests that there is danger that too many residencies may be developed and stresses that, in the best interests of the patient, high quality of teaching in the residency is now more important than a large increase in the number of residencies. The essentials of a satisfactory residency are listed in some detail, although the Commission takes pains to point out that it does not wish to standardize residencies or put them in a straitjacket.

Postgraduate education the Commission defines as study intended to keep a physician abreast of his chosen field of practice but not intended to equip him to enter a new field. Separate and clearly defined types of work are recommended for general practitioners and for specialists. While there has been a marked and rapid increase in interest in the field of postgraduate medical education, there is still need for its further extension and for improvement in the type of opportunities offered. The report points out the advantages and disadvantages of the various types of training now provided.

The effect of the work of the specialty boards upon the practice of medicine is discussed in the report, which points out that these boards have provided a well defined yardstick for measuring an individual physician's competence in his specialty. Men in the specialties have been certified so rapidly that it soon will be possible for the great majority of the people of this country to have access to the services of certified specialists.

The entire report stresses the value of adequate training and points out that this will be reflected in improved care of patients.

PLACEMENT BUREAU FOR ROENTGEN-RAY TECHNICIANS

As a means of facilitating contact between roentgen-ray technicians and radiologists in need of the services of competent roentgen-ray technicians The American Registry of X-Ray Technicians has put into operation a Placement Bureau. This Bureau will act as a clearing-house for roentgen-ray technicians, and is designed to expedite the procedures of bringing employer and technician together.

Roentgen-ray technicians applying for Placement Service will be classified according to their added abilities as nurses, laboratory technicians, etc., and those having the particular qualifications specified by a radiologist registering a vacancy with the Bureau will be advised where and when to apply for the position. It is hoped that by centralizing this employment function much needless correspondence and investigation on the part of the radiologist can be eliminated.

The Placement Bureau will function without fee to either employer or employee and will be limited in scope to registered

technicians in good standing and physician-radiologists of approved rating. Radiologists wishing to avail themselves of the services of the Placement Bureau may register their vacancies by writing to Alfred B. Greene, R. T., Executive Secretary, American Registry of X-Ray Technicians, Oak Terrace, Minnesota.

ANNOUNCEMENT OF THE JOURNAL OF THE NATIONAL CANCER INSTITUTE

The National Cancer Institute, of the National Institute of Health, United States Public Health Service, announces the forthcoming issue of *The Journal of the National Cancer Institute*, the official organ of the Institute.

The new Journal, which will be issued bimonthly, will be of the scientific type of periodical, and will contain articles by the members of the staff on the various lines of cancer research work carried on by the Institute.

The first issue will include papers on the Federal cancer control program, the approaches to cancer research, the effect of various hydrocarbons in producing tumors in mice, and studies on normal and cancerous tissues.

Copies of the Journal will be sold to applicants by the Superintendent of Documents, Government Printing Office, Washington, D. C., who will also handle all annual paid subscriptions. The price of subscription will be $3.00 a year in the United States.

The Journal will be distributed free to a limited number of medical schools, to workers in the field of cancer research, to research institutes interested in cancer, to a limited number of surgeons, as well as to certain Government depositories, and to journals making suitable exchanges.

GRADUATE TRAINING IN RADIOLOGY

Graduate training in radiology for a period of three full-time academic years is available at the New York University College of Medicine to a limited number of young physicians who have completed internships. The course of study is designed to meet the requirements of the American Board of Radiology and includes training in the basic medical sciences and two years of work in the Department of Radiology of the College. Other details may be obtained from the Office of the Dean, 477 First Avenue, New York.

DR. CHAMBERLAIN HONORED

Dr. W. Edward Chamberlain, who ended a five year term as Chairman of the Board of Chancellors of the American College of Radiology at its annual meeting in New York on June 12, was voted a signal honor by the Fellows of the College present at the annual banquet. A resolution submitted by Dr. E. P. Pendergrass, Philadelphia, to confer the gold medal of the American College of Radiology upon Dr. Chamberlain was unanimously adopted. The gold medal of the College has previously been presented only to Honorary Fellows. Dr. William D. Coolidge, Dr. Charles C. Lauritsen, Dr. H. Clyde Snook, Dr. Albert Soiland, and Madame Marie Curie have been thus honored. Dr. Pendergrass called attention to "his tireless effort and boundless enthusiasm, which has brought the College to a position of strength and usefulness beyond that which we even hoped for when he assumed office five years ago," in moving the adoption of his resolution to confer the gold medal upon Dr. Chamberlain.

AMERICAN COLLEGE OF RADIOLOGY

The following officers were elected at the annual meeting of the American College of Radiology, held at the Commodore Hotel in New York City on June 12, 1940: President: Dr. Henry J. Walton, Baltimore, Maryland; Vice-President: Dr. Sherwood Moore, St. Louis, Missouri; Chairman, Board of Chancellors: Dr. Vincent W.

Archer, University, Virginia. New members of the Board of Chancellors elected for a four-year term were: Dr. Lewis G. Allen, Kansas City, Kansas; Dr. George E. Pfahler, Philadelphia, Pennsylvania. Dr. Hollis E. Potter, Chicago, was re-elected Treasurer, and Mr. Mac F. Cahal was re-elected Executive Secretary.

The next annual meeting of the College will be held at Cleveland on Wednesday during the week of the meeting of the American Medical Association.

CHICAGO ROENTGEN SOCIETY

At a recent meeting of the Chicago Roentgen Society the following officers were elected for the coming year: *President:* Dr. Adolph Hartung; *Vice-President:* Dr. Warren W. Furey; *Secretary-Treasurer:* Dr. Chester J. Challenger. Meetings are held on the second Thursday of each month from October to April inclusive at the Palmer House, Chicago.

INDIANA ROENTGEN SOCIETY

The annual meeting of the Indiana Roentgen Society was held in Indianapolis on May 19, 1940. After the dinner, the guest speaker, Dr. E. A. Pohle, read a paper on "Radium Treatment of Vascular Nevi." The following officers were elected for the coming year: *President:* Dr. H. H. Inlow, Shelbyville; *President-Elect:* Dr. Charles Wyeth, Terre Haute; *Vice-President:* Dr. C. A. Stayton, Indianapolis; *Secretary-Treasurer:* Dr. Clifford C. Taylor, Indianapolis.

RADIOLOGICAL SOCIETY OF NEW JERSEY

At the recent meeting of the Radiological Society of New Jersey held on June 5, 1940, in Atlantic City, the following officers were elected for the ensuing year: *President:* Dr. James G. Boyes, Plainfield, N. J.; *Vice-President:* Dr. Nathan J. Furst, Newark, N. J.; *Secretary:* Dr. W. James Marquis, Newark, N. J.; *Treasurer:* Dr. H. A. Vogel, Elizabeth, N. J.; *Counsellor:* Dr. H. J. Perlberg, Jersey City, N. J.

OHIO RADIOLOGICAL SOCIETY

At the recent annual meeting of the Ohio State Medical Association the radiologists of Ohio met at a business dinner meeting, the purpose of which was to organize a State Radiological Society. The meeting was well attended. The following officers were elected: *President*, Dr. U. V. Portmann, Cleveland; *Secretary*, Dr. J. E. McCarthy, Cincinnati. A committee was appointed to draw up a constitution and by-laws. The next meeting will be held at the time and place of the annual meeting of the Ohio State Medical Association.

PACIFIC ROENTGEN SOCIETY

At the annual meeting of the Pacific Roentgen Society held at Coronado in May 1940, the following officers were appointed for the ensuing year: *Chairman:* Dr. William E. Costolow, Los Angeles; *Secretary-Treasurer:* Dr. L. H. Garland, San Francisco; *Members of the Executive Committee:* Dr. I. S. Ingber, San Francisco, Dr. D. R. MacColl, Los Angeles, Dr. J. D. Coate, Oakland. The Executive Committee meets quarterly; the Society meets annually, during the annual meeting of the California Medical Association.

PITTSBURGH ROENTGEN SOCIETY

At a recent meeting of the Pittsburgh Roentgen Society, the following officers were elected: *President:* Dr. Paul G. Bovard, Tarentum, Pa.; *Vice-President:* Dr. John H. Gemmell, Rochester, Pa.; *Secretary-Treasurer:* Dr. Harold W. Jacox, Pittsburgh, Pa. Meetings are held the second Wednesday of each month at 4:30 P.M. from October to June at various hospitals designated by the Program Committee.

Vol. 44, No. 2

DEPARTMENT OF TECHNIQUE

Department Editor: Robert B. Taft, M.D., B.S., M.A., 105 Rutledge Ave., Charleston, S. C.

APPLICATION OF DENTAL MOLDS TO RADIUM THERAPY*

By LOUIS J. LEVINSON, B.S., M.D., *and* NATHAN PECK, B.S., D.D.S.
NEWARK, NEW JERSEY

IN THE treatment of oral neoplasms with radium applicators the use of molds is often necessary. Until one year ago these molds were made in our clinic from dental compound. The type used was a direct mold obtained by heating dental impression compound, molding to fit the shape of the mouth, and using the resulting product as our final appliance. The radium needles or capsules were then embedded in the compound and the mold was inserted for the required period of time.

Numerous difficulties were encountered when using this type of mold. The process of embedding the capsules required heat, which often distorted the mold. The determination of the exact distance of the radium capsules from the lesion was difficult. The patient had to be present during the entire procedure for necessary adjustments. When worn for several days a mold of this type frequently caused marked irritation.

The obvious crudeness of this method induced us to utilize a more refined technique. The method we are now employing is similar to that used by the dental profession in making prosthetic appliances, indirectly, from exact models of the mouth.

TECHNIQUE

Impression. A metal impression tray is selected to fit the size and shape of the patient's mouth. Dental impression compound of the type which can be obtained in any dental supply store is made plastic by heating in water at 56° C. The impression tray is then carefully filled with compound and placed in the patient's mouth. Since the compound remains plastic for a few minutes, the operator's fingers can quickly mold the compound around the lesion. The tray and compound are then removed and chilled in ice water. The result (Fig. 2) is a clear negative imprint of the patient's mouth. The patient is now dismissed until the mold is completed.

Model. The model is made by pouring cast stone into the impression. This material is a powder and consists chiefly of plaster of paris ($CaSO_4 \cdot 2H_2O$) which has been refined and calcined, and to which are added certain proprietary hardening agents. A mixture of cast stone and water is semi-solid, flows easily and readily takes the shape of the impression into which it is poured. Upon setting, a hard dense stone-like model is formed which has the desirable property of not fracturing easily. The impression compound is now removed from the stone model by melting it away with hot water. After trimming, the result is a permanent positive reproduction of the jaw and lesion (Fig. 2).

MAKING THE MOLD

A. The Base Plate. This consists of a shellac fiber material, about 1 mm. in thickness, which can be made plastic by the application of dry heat. Such a shellac base plate is made plastic with the Bunsen flame and closely adapted to the model with the fingers of the operator. After

* From the Tumor and Dental Clinics of the Newark Beth Israel Hospital.

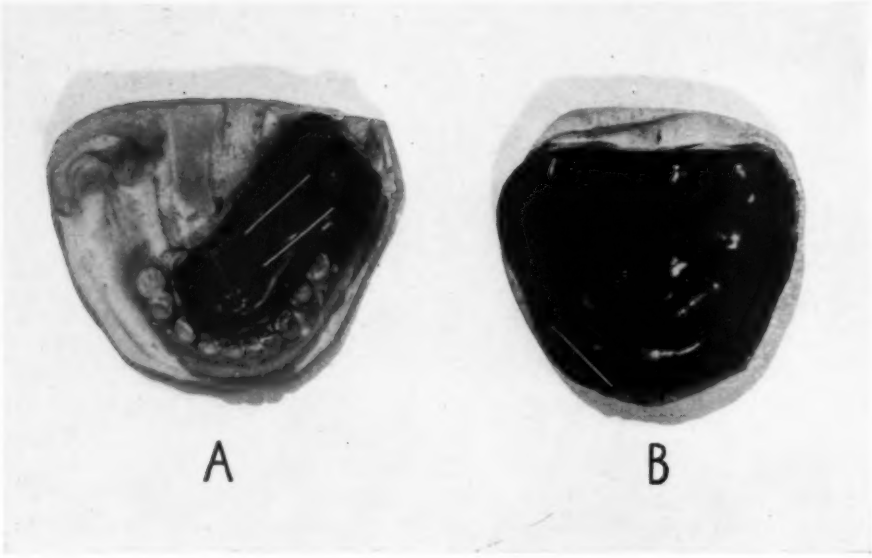

Fig. 1. *A*, mold with radium attached; *B*, type of mold used in edentulous cases.

chilling, there results a thin, smooth, closely fitting negative replica of the tissues, not unlike the tissue bearing portion of a completed oral prosthesis (Fig. 2). Base plate material is admirably suited for this purpose, as it is easily molded in the

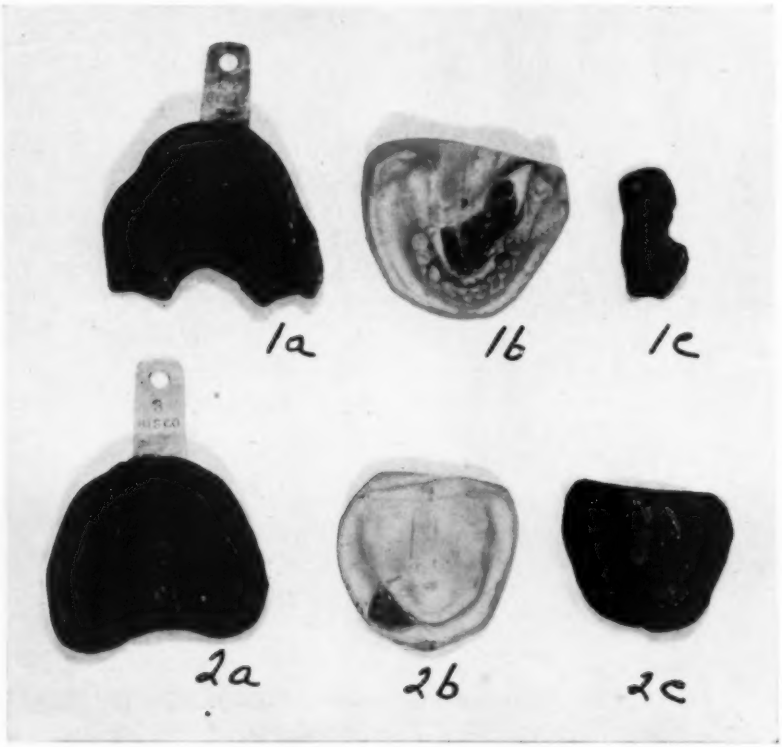

Fig. 2. 1*a*, 2*a*, the impression; 1*b*, stone model of a carcinoma of floor of mouth; 2*b*, stone model of an epulis of upper alveolar ridge; 1*c*, 2*c*, base plates, 1 mm. in thickness.

heated state and maintains a uniform thickness. In cases where several teeth remain near the lesion, the base plate is made sufficiently large to cover the area involved. In edentulous patients we have found it advantageous to cover the entire dental ridge (Fig. 1).

B. Reënforcing and Securing Lesion Distance. The base plate replica is replaced upon the model. Impression compound of the same type used in taking the original impression is now used in reënforcing the base plate and in obtaining the proper spacing of the radium capsules from the lesion. The compound is made plastic in hot water and the required thickness is molded to the outer surface of the base plate. After chilling, the edges of the compound and base plate are seared together with a hot spatula (Fig. 1).

C. Placing the Radium. The area covering the lesion is outlined on the compound-bearing surface of the mold. The mold is then replaced upon the model, the outlined area gently heated with the Bunsen flame, and the required number of radium applicators are attached to the softened area of the compound (Fig. 1).

D. Protection of Proximate Tissues. Additional impression compound is again made plastic and placed over the radium applicators. This assures fixation of the radium to the appliance, and in addition provides much protection to the adjacent soft tissues by pushing them away from the radium surface of the mold. In addition, lead foil may be used for further protection.

E. Inserting the Appliance. At this stage the patient is recalled. The appliance is hardened in ice water and inserted like any ordinary prosthesis for the duration of treatment prescribed.

CONCLUSIONS

There are definite advantages in the use of the indirect method over the old direct method of making oral radium molds. These advantages compensate for the additional time and effort involved in the use of the indirect procedure. The advantages are as follows:

1. A permanent record in the form of a stone model is obtained.

2. A minimum of clinic time is necessary in actually dealing with the patient. Once an impression is made the patient is dismissed and the mold is completed at the technician's convenience.

3. A predetermined exact distance of the radium applicators from the lesion can be readily obtained.

4. A homogeneous distribution of the radium over a designated area can be more accurately planned by comparing the outline on the mold with the lesion as shown by the stone model.

5. The indirectly made appliance is smoother and better fitting and is thus well tolerated by the patient when prolonged irradiation is necessary.

6. The mold is easily removed for feeding by patient or nurse and can be replaced like any other prosthesis.

INDEX TO ABSTRACTS

ROENTGEN AND RADIUM THERAPY

Newell, E. T., Jr.: Carcinoma of the lip..... 307

Engelstad, R. B.: Radiation treatment of carcinoma of the lip..... 307

Possati, A.: Roentgen treatment of leukemia with changeable filters..... 307

Siciliano, L.: Roentgen treatment of polycythemia..... 308

Schaefer, W., and Huber, H.: A new roentgen method employed in climacteric hemorrhages with sparing of the ovaries..... 308

v. Kövesligethy, I.: Radiation therapy of urethral carcinoma..... 309

Simon, O.: Treatment of polycythemia with irradiation of the entire body..... 310

Ponzio, M.: The value and limitations of radium and roentgen treatment in acute inflammatory processes..... 310

Chaoul, H., and Greineder, K.: Treatment of deep infiltrating carcinoma by means of close irradiation..... 311

Greineder, K., and Neumann, W.: New results regarding the close irradiation of malignant melanoma..... 311

von Wieser, W.: Roentgen therapy of multiple sclerosis..... 312

Horvath, J.: Roentgen treatment of carcinoma of the skin and lip..... 313

Pagani, A.: The benign vascular tumors of the region of the parotid and their treatment with radium moulage..... 313

Pellegrini, G.: Roentgen therapy of the thyroid gland in the treatment of cardiac decompensation..... 314

Glauner, R., Teufel, S., and Daigger, A.: Results from protracted fractional roentgen irradiation of carcinoma of the upper respiratory and food passages..... 315

Wessely, E.: Therapy of carcinoma of the vallecula..... 316

Reichenmiller, H.: Individual radium treatment in carcinoma of the uterine cervix... 316

Kirchhoff, H.: Fractional roentgen irradiation of advanced carcinoma of the cervix with involvement of the efferent urinary passages..... 317

Goecke, H.: Results from treatment of carcinoma of the uterus..... 318

MISCELLANEOUS

Inouye, K.: Biological effect of alpha rays in consideration of the problems of weak radium therapy..... 318

Bade, H., and Küntscher, G.: Action of roentgen rays on the bones..... 319

Gregori, A.: Effect of roentgen rays on the bone marrow "in vivo" and "in vitro".... 319

Sutro, C. J., and Pomerantz, L.: Effect of experimentally formed tumors on the musculoskeletal system of the rat..... 320

Harrington, H. L., and Huggins, C.: Rate of removal of thorium dioxide from the blood stream..... 320

Miyamoto, S.: Experimental sarcoma production by thorotrast..... 320

Toniolo, G.: Effect of roentgen rays on Galliera sarcoma in vivo and in vitro..... 321

Bade, H.: Roentgen-ray sensitiveness of the skin as dependent on the central and peripheral nervous systems..... 322

Bade, H.: Is it possible to demonstrate an influence of roentgen radiation on striated musculature when the tolerance threshold of the skin is exceeded?..... 322

Luther, W.: Effect of roentgen rays on cell division..... 322

Langendorff, H., and Papperitz, W.: Effect of a single roentgen dose on the bone marrow of a white mouse..... 323

ABSTRACTS OF ROENTGEN AND RADIUM LITERATURE

ROENTGEN AND RADIUM THERAPY

Newell, Edward T., Jr. Carcinoma of the lip. *Arch. Surg.*, June, 1939, *38*, 1014–1029.

This is a clinical and pathologic study of 390 cases of carcinoma of the lip treated surgically. Of these, 344 were squamous cell carcinomas, 44 basal cell carcinomas, and 2 adenocarcinomas. The incidence of basal cell carcinoma of the lower lip was 2 per cent and that of basal cell carcinoma of the upper lip 67 per cent. There were 344 lesions of the lower lip and 54 of the upper lip. The incidence of metastases or recurrences when first seen was 36 per cent.

To determine five year end-results, the cases were divided into three groups according to treatment received: Group one, local excision alone; group two, local excision plus dissection of the cervical nodes in which no metastases were found microscopically; group three, cases in which both local excision and cervical gland dissections were done in which metastases were found. The percentage of five year cures was: group one, 81 per cent, group two, 85 per cent, and group three, 23 per cent.—*P. J. Hodes.*

Engelstad, Rolf Bull. Radiologische Behandlung des Lippenkarzinoms. (Radiation treatment of carcinoma of the lip.) *Strahlentherapie*, 1939, *64*, 571–589.

1. Radiation treatment of the primary tumor is more effective in carcinoma of the lip than surgical treatment. In the cases treated by the author the disappearance of local symptoms was obtained in all cases where the tumor was small and in all large operable tumors with the exception of one case; at the same time a disappearance of symptoms was obtained in over one-third of the inoperable cases. The cosmetic result is infinitely better with radiation treatment. This author is of the opinion, therefore, that primary tumors of the lip should always be treated primarily radiologically, since the results are not as satisfactory when radiation treatment is employed only when a recurrence takes place following surgical treatment. The author doubts whether better results could be obtained by primary surgery and followed by roentgen irradiation.

2. In the treatment of lymph node metastases, the relations are considerably more complex and satisfactory results are not always obtained by radiation treatment alone. In cases of this type the author employs at first teleroentgen treatment. If the lymph node metastases do not subside after this treatment or if a recurrence takes place, a total extirpation of the cervical lymph glands is carried out where possible. The author recommends this type of treatment on the basis of the good results obtained by him.

3. In cases where no palpable lymph nodes are present or where the lymph nodes are enlarged but do not give the impression of being metastatically affected, no prophylactic treatment is employed. In cases of this type, however, repeated periodic examinations are necessary.

4. In the cases treated according to the methods outlined above, the following results were obtained: A disappearance of symptoms in 68.2 per cent under an observation of three to six years' duration, a value which compares favorably with other methods of treatment. The advantages of this method consist in the absence of unpleasantness, a decrease to a minimum of the danger of infection and a limitation of the local reactions due to the irradiation.—*A. Schwartzman.*

Possati, Alberto, Die Röntgenstrahlenbehandlung der Leukämie mit veränderlichen Filtern. Ein Sonderverfahren in einigen Krankheitsabschnitten. (Roentgen treatment of leukemia with changeable filters. A special procedure in some phases of the disease.) *Strahlentherapie*, 1939, *65*, 54–58.

Even though a good deal has been written regarding the roentgen treatment of leukemia, nevertheless the author believes he is justified in the presentation of this communication since he is of the opinion that in certain cases the results obtained by him were very satisfactory. This report deals exclusively with myeloid leukemia. The method of treatment employed by this author consisted in a careful irradiation

of the liver and spleen with very small amounts, at times with a fraction of the skin erythema dose, carried out in the course of weeks with very slight interruptions. In this manner it was possible not only to improve the general condition of the patient, but to maintain the patient alive from two to three years longer than it would be possible otherwise.

Every roentgenologist is familiar with the fact that in some instances splendid results have been obtained at times with very distinctly different methods of treatment; similarly most roentgenologists are familiar with the refractory cases. The difference regarding the quality and quantity of the rays employed varies from case to case, but on the whole, cases of myeloid leukemia were found to respond to roentgen treatment irrespective of its type. No given scheme is available for the treatment of all cases. In each case the treatment must be strictly individualized. In many instances the general condition of the patient is of significance and is of more importance than the blood picture. Patients are met with who have been subjected to roentgen treatment by different roentgenologists with variable results. In some instances, because of repeated roentgen treatment the patient becomes practically non-responsive or non-sensitive to the roentgen rays. In the last mentioned type of cases, satisfactory results were obtained by this author from the use of changeable filters. This was especially true for the cases which were previously treated by different roentgenologists and which later appeared refractory to roentgen rays. Using this method of treatment, satisfactory results were obtained by the author even in patients with a very poor general condition and otherwise severely ill. The author is of the opinion that this type of treatment would prove of value also in suitable cases of lymphogranuloma.—*A. Schwartzman.*

Siciliano, L. Die Röntgenbehandlung der Polyzythämie (Roentgen treatment of polycythemia.) *Strahlentherapie*, 1939, *65*, 100–107.

Total roentgen therapy is the method of choice in the treatment of polycythemia. A study of the literature reveals that the roentgen treatment of this disease by other methods is not effective. Best results have been obtained only in recent years since teleroentgen therapy has been employed. However, even in the employment of this technique of irradiation, its limitations and dangers must always be remembered. In each case the blood picture must be carefully controlled in order to determine the threshold of inquiry. In a case treated by the author in the course of two years, the following technique was employed. The irradiation was carried out at a distance of 70 cm. Only the genitals were protected during the irradiation of the hips. The irradiation was given under a tension of 160 kv., 4 mm. Al filter and 3 ma. The irradiation was begun with doses of 15 r after which the doses were gradually increased to 70 r per treatment. The effect of irradiation began to be observed six weeks after the treatment was instituted. If irradiation is discontinued the blood values return to normal in about six months at which time the irradiation must be repeated. Throughout the irradiation, special attention must also be paid to the behavior of the white blood corpuscles. On the basis of his observation this author comes to the following conclusions:

1. The radiation must be applied to most of the bone marrow but not to the back. Under these conditions the doses employed must be considerably larger than in genuine total irradiation and necessarily a longer time elapses before changes in the blood picture appear. The author believes that irradiation under a tension of 160 kv. with a 4 mm. filter is sufficient. Using this method of irradiation the danger of the appearance of anemia and hemorrhagic symptoms is not very great.—*A. Schwartzman.*

Schaefer, W., and Huber, Herbert. Über eine neue Röntgenmethode bei klimakterischen Blutungen mit Schonung der Ovarien. (A new roentgen method employed in climacteric hemorrhages with sparing of the ovaries.) *Strahlentherapie*, 1939, *64*, 557–570.

The hitherto employed methods in the treatment of climacteric hemorrhages are: atmokausis, percutaneous roentgen irradiation of the ovaries, and intrauterine radium irradiation. The atmokausis, previously frequently employed and then practically completely discarded, has recently begun to be employed more and more frequently; a new apparatus for this type of treatment has recently appeared on the market. This method was originally discarded for a number of reasons, but chiefly because it was found that frequently it was impossible to destroy the mucosa by means of the

vapor, the treatment was frequently ineffective and the hemorrhages frequently recurred. Other objections were based on the fact that adhesions occasionally developed as a result of the destruction of the cervical mucosa and these adhesions interfered with the outflow of the uterine secretion and blood and frequently led to the development of hematometra and pyometra. As contrasted with this method of treatment, roentgen treatment appeared less dangerous and infinitely more reliable; it is not surprising, therefore, that the latter began to be employed practically exclusively for the treatment of climacteric hemorrhages.

At present besides roentgen irradiation of the ovaries with a given dose, intrauterine radium irradiation is frequently employed. This type of irradiation is directed chiefly, just as in the vaporization, towards the destruction of the mucosa of the uterus but practically retains the function of the ovaries and consequently the symptoms due to loss of function are either reduced or greatly minimized. However, good results are obtained from the radium treatment only where relatively large doses are employed. According to the experience of this author, at least 2,000 mg-hr. of radium are necessary in order to obtain satisfactory results. The size of the uterus and consequently the size of the uterine cavity are of significance. In cases where the uterus is small, a smaller dose will suffice, while in cases where the uterus is large a considerably larger dose is necessary. The effect on the ovaries varies depending on the proximity of the radium to the ovaries. In general, however, the more distantly situated ovaries are affected only to a slight extent by the radium although the parts of the ovaries situated proximal to the uterus are as a rule affected by the radium.

This author believes that he has eliminated the objections to percutaneous roentgen treatment of the ovaries and intrauterine radium treatment of the ovaries for purposes of controlling climacteric hemorrhages by the use of a roentgen tube which is introduced directly into the uterine cavity. The dose of roentgen rays used in these cases is about 200 r. He believes that this method is preferable to the methods hitherto employed. Its advantages over the radium treatment are based on the fact that it spares the ovaries no less than the radium, there is less danger of injury to the bladder and the complete treatment is achieved in the course of one hour instead of twenty to forty hours as in radium.—*A. Schwartzman.*

v. Kövesligethy, Ivan. Die Strahlentherapie des Urethralkarzinoms. (Radiation therapy of urethral carcinoma.) *Strahlentherapie*, 1939, *64*, 613–618.

In the treatment of carcinoma of the urethra the radical surgical measures employed in carcinoma of the vulva are not applicable; urethral carcinoma is also more malignant than carcinoma of the vulva. It is one of the rarest types of carcinoma. Between 1920 and 1935 only 16 cases of carcinoma of the urethra out of 1,914 cases of carcinoma in general were observed and treated by this author in his gynecologic clinic. It appears as a rule in advanced age but is not rare in relatively young individuals. The age distribution in the cases studied by the author was as follows: 6 between forty and fifty, 4 between fifty and seventy, 4 above seventy and in 2 below forty.

Depending on its localization carcinoma of the urethra may come to manifestation either as a genuine carcinoma of the urethra, as a vulvo-urethral carcinoma and as a peri-urethral carcinoma.

Histologically carcinoma of the urethra appears most commonly as an epithelial carcinoma and occasionally as a glandular carcinoma. In advanced cases the diagnosis is relatively easy. In the early stages the diagnosis must be based on histologic examination.

The symptoms of urethral carcinoma are pain, hemorrhage and difficulty of urination, burning on urination. The symptoms become progressively worse with the progress of the disease.

In the treatment of carcinoma of the urethra, surgery, radiation therapy, and a combination of the two methods are employed. Surgery, as well as radiation treatment, is technically difficult to carry out in these cases. In the surgical treatment a partial resection as well as a total extirpation of the urethra is employed. Judging by the results reported in the literature, a partial resection only rarely gives satisfactory results. Total extirpation of the urethra gives a high primary mortality. Surgical treatment in cases of this type cannot be considered satisfactory. According to most of the statistics found in the literature, only 5 per cent of the surgically treated cases are free of recurrences during five years and only 20 per cent of the

operated cases survive the operation by one year. Somewhat better results are obtained from the combined surgical and roentgen treatment, but in general here also the results cannot be considered as satisfactory. This author believes that he has obtained more satisfactory results from the radium treatment of urethral carcinoma. In 62.5 per cent of the cases treated by him, a palliative effect of one year duration was obtained while in 16.6 per cent of the cases a cure of ten years' duration in one and of six years' duration in another was obtained.—*A. Schwartzman.*

Simon, O. Zur Polyzythämiebehandlung mit Körpenganzbestrahlungen. (Treatment of polycythemia with irradiation of the entire body.) *Strahlentherapie*, 1939, *65*, 424–430.

The technique of irradiation of the entire body employed by the author was carried out according to the method of W. Teschendorf with 4 ma, 180 kv., 0.5 mm. copper filter and a focus-skin distance of 150 cm. The irradiations were carried out with daily doses of 7 to 28 r alternating the dorsal and frontal parts of the body. The genital organs and the eyes were protected by means of lead covers from the direct rays.

Immediately after irradiation there was observed in some cases an intensification of the subjective symptoms. This intensification was apparently the result of the increased discharge of the blood cells from the bone marrow into the circulation. In individual cases irradiation was followed by a transitory increase in the number of red and white cells. After the fourth to the sixth irradiations there occurred in all cases a definite decrease in the intensity of the symptoms which frequently preceded a decrease in the number of red cells.

In about one-third of the cases the white cell count was normal prior to irradiation while in about two-thirds of the cases the white cell count varied between 11,000 and 25,000. In practically all cases the differential count showed a more or less pronounced shift to the left with the appearance of young forms and occasionally also of myelocytes as well as a considerable lymphopenia. A decrease in the leukocyte count was observed eight to twelve days after the beginning of irradiation. This decrease continued in some cases even after the irradiation was terminated during the following two to three weeks reaching at times a value of 2,000 cells. A leukopenia of this type is associated neither with a disturbance of the general condition nor with any pathological signs or symptoms.

A decrease in the hemoglobin and red cell count occurred in some cases simultaneously with the decrease in the number of leukocytes while in other cases it appeared only one to two weeks later. This decrease continues somewhat longer after the termination of the irradiation than the decrease of the white cells. In some cases even a slight degree of anemia may be produced.

In each of the treated cases the whole body irradiation was followed by return to normal of the red blood picture and a complete disappearance of the symptoms. The duration of the remission lasted in most of the cases from two to five years. The duration of the remission is apparently independent of the conditions of irradiation such as intensity of the rays or daily dose. It was observed that there seems to exist a parallel between the results obtained and the degree of decrease of the leukocyte count observed following the termination of the irradiation. In cases where no demonstrable decrease of leukocytes was observed the remission was as a rule of short duration.—*A. Schwartzman.*

Ponzio, Mario. Ueber den Wert und die Grenzen der Radium-Röntgenbestrahlung bei akuten Entzündungsprozessen. (The value and limitations of radium and roentgen treatment in acute inflammatory processes.) *Strahlentherapie*, 1939, *65*, 195–203.

Hitherto the therapeutic use of rays of short wave length of the spectrum in acute inflammatory diseases was mostly empirical in nature; nevertheless already at the beginning of the present century, attempts had been made to influence inflammatory processes, especially suppurative processes of glands, by means of roentgen rays; they were found effective in many instances. Domenicis reported obtaining satisfactory results from the use of radium therapy in the treatment of subacute gonorrheal arthritides. Cheron reported very satisfactory results from the use of roentgen treatment in adnexal and periadnexal inflammations.

Somewhat later numerous attempts were made to determine experimentally the reason for the improvement obtained from this type of treatment. The experimental studies of Holweck and others have shown that in certain bacterial ele-

ments the cell destruction is achieved by the absorption of certain types of rays. Further studies have shown, however, that the reaction ability varies with the cellular element. In other words, the effectiveness of the roentgen treatment depends on the state of function of the given cell. It was further found that besides the bactericidal property of the roentgen rays and radium rays, the beneficial effect also results from a secondary activation of the protective properties of the tissues proper, the latter in its turn depending on the condition of the tissues in general.

It is generally agreed at present, however, that in each case the effect of irradiation must be looked upon as essentially local in nature while the plasma changes and the increased bactericidal effect of the tissues is only secondary. It has also been found that under the influence of roentgen and radium irradiation there occur definite vascular changes. These vascular changes have been demonstrated by capillary microscopic studies and clinically are manifested in the form of erythema. A definite response is also obtained from the reticulo-endothelial system found in the various tissues of the body.

On the basis of all these findings Ponzio comes to the conclusion that the therapeutic effect resulting from roentgen and radium irradiation of inflammatory processes is dependent on the increase in the immunological properties of the reticulo-endothelial system and the vascular changes in the region of the inflammation proper.—*A. Schwartzman.*

Chaoul, H., and Greineder, K. Die Behandlung tiefinfiltrierender Krebse mit der Nahbestrahlung. (Treatment of deep infiltrating carcinoma by means of close irradiation.) *Strahlentherapie*, 1939, *66*, 73–88.

The opinion has been expressed by some authors that close irradiation is suitable only for the treatment of superficial carcinoma. This erroneous assumption is due to the fact that it has been thought that with the increased extension and depth of the carcinoma also the percentage dose must be correspondingly higher; consequently it appeared illogical to use this type instead of deep therapy for deep infiltrating tumors.

Reasoning of this type is the result of the assumption that the rays act only in one plane. Studies have shown, however, that in close irradiation one deals with the correlated effect of distinct individual features which supplement and complement each other.

These authors treated 264 cases of skin carcinoma by the close method of irradiation. Of these 264 cases, in 211 the tumor was of the non-infiltrating and in 53 of the infiltrating type; 14 cases presented regional metastases. Using the close method of irradiation a disappearance of all symptoms was obtained in 207 of the 211 non-infiltrating cases, that is, in 98 per cent and in 41 of the 53 infiltrating cases, or 77.3 per cent.

The same method of treatment was employed in 61 cases of carcinoma of the lip; in 50 the lower lip and in 11 the upper lip was affected. In 35 cases the tumor was non-infiltrating and in 26 cases it was infiltrating in type. In 20 regional metastases were present. A primary and complete disappearance of symptoms was obtained in 33 of the 35 non-infiltrating cases, that is, in 94.2 per cent, and in 21 of the 26 infiltrative cases, or 80.7 per cent.

One hundred and eighteen of the patients with carcinoma of the skin were observed from three to seven years. In 89 the carcinoma was non-infiltrating and in 29 it was infiltrating in type; 80 of the 89 cases were cured and 17 of the 29 cases were cured. Thirty of the patients with carcinoma of the lip were observed from three to seven years; 13 of these were of the infiltrating type and 17 of the non-infiltrative type; 16 of the 17 non-infiltrating cases were cured and 8 of the 13 infiltrating cases. A comparison of the data presented above with comparable data of other authors shows clearly the suitability of close irradiation for the treatment of non-infiltrating as well as infiltrating carcinoma of the skin and lip.—*A. Schwartzman.*

Greineder, Kurt, and Neumann, Werner. Neue Ergebnisse über die Nahbestrahlung des malignen Melanoms. (New results regarding the close irradiation of malignant melanoma.) *Strahlentherapie*, 1939, *66*, 89–95.

Malignant melanoma is one of the most feared types of carcinoma. It is characterized by an unusual ability of infiltrative growth and by a strong tendency to early metastasis. Various methods of treatment have been employed in an attempt to combat this type of tumor, namely, purely surgical excision, electrosurgical treatment by electrocoagulation, or electroendothermy, roentgen irradiation, radium ir-

radiation, or various combinations of surgical and radiological treatment. The results obtained from these various treatments by various authors as reported in the literature are varied and are not quite comparable. For a number of years Greineder and Neumann have treated malignant melanoma by the close irradiation method. The results obtained were at first reported in 1936 at the Roentgenological Conference in Wiesbaden. At that time they were able to show that it is possible to achieve a disappearance of a malignant melanoma by means of close irradiation even in the cases where the melanoma up to then appeared resistant to roentgen and radium rays. A complete disappearance of the tumor was obtained in a series of patients even after the original report was made.

In this article Greineder and Neumann briefly discuss the fate of the patients reported in 1936. One of the 14 patients must be excluded from the discussion because this was a case of a recurrence following surgical removal. Of the remaining 13 patients no follow-up could be carried out of 2 patients after two years of observation during which time they appeared clinically cured. In one patient a regional metastasis appeared after five and a half years and 4 other patients have died since the original report was made. At present, therefore, 6 of the original 13 patients are still completely free of symptoms.

The present report deals with a study of 25 patients. In some of these patients the tumors were present for a long time and in 5 regional metastases were present when first seen. Of a total of 25 patients a primary complete disappearance of symptoms was obtained in 22, or 88 per cent. The lack of symptoms regarding the duration of observation was as follows: in 2 patients after five years of observation, in 4 from four to five years of observation, in 4 from three to four years, in 6 from two to three years, in 4 from one to two years and in 5 the observation period was below one year. Of the 25 patients, 16 were free of symptoms after two years and 10 were free of symptoms after three years.

Also the 5 patients with the regional metastases on admission were treated by the principles of short distance irradiation. Two of these have died while in 2 others the glandular swelling disappeared completely. The duration of observation of these patients varied from three years and seven months to five years. The fifth patient has been under observation for two years and during this time has presented only a slight hardening of the gland.

The results presented above clearly show that even patients with regional glandular metastases may be kept alive for years when the close method of irradiation is employed. The results are not as satisfactory in cases of recurrences following surgical treatment. Where possible, surgery should be avoided. In some instances, however, even surgical recurrences are very favorably influenced. These authors are of the opinion that the primary close irradiation of malignant carcinoma is a very satisfactory method of treatment of this type of tumor. In at least 50 per cent of the cases a cure at least of one year duration is obtained by this method.—*A. Schwartzman.*

VON WIESER, W. Zur Röntgentherapie der multiplen Sklerose. (Roentgen therapy of multiple sclerosis.) *Strahlentherapie*, 1939, *65*, 283–303.

A study of the literature dealing with the subject reveals that over 25 communications have appeared in which the favorable results of roentgen treatment of multiple sclerosis were reported in 264 cases. The same study reveals that this type of treatment was instituted as early as 1902. Since 1924 the subject has been frequently studied and reported by many authors.

Multiple sclerosis is generally considered as one of the most frequent organic nerve diseases. The constant objection to the evaluation of the results obtained from roentgen treatment of multiple sclerosis is based on the frequent spontaneous remissions which at times last for years, as a result of which it is apparently impossible to determine with certainty whether the improvement obtained is due to the treatment or whether it represents a spontaneous remission coincidental with the institution of treatment. It is apparent from the above that in a given case it is frequently absolutely impossible to demonstrate with certainty whether one is dealing with a spontaneous remission or with an improvement resulting from treatment. However, the average remissions observed in a given number of cases not treated by roentgen radiation are not as frequent as the improvement obtained in a similar number of cases treated by roentgen radiation, indicating, therefore, that the improvement in many cases is no doubt due to the roentgen treatment and is not the result of spontaneous remission.

There is no doubt whatever that in a very large number of cases roentgen therapy of multiple sclerosis produces at least a temporary improvement and since the condition is as a rule refractory to any other form of treatment, even the temporary improvement justifies the use of this type of therapy.

This author treated personally a number of cases of multiple sclerosis by means of roentgen rays. On the basis of the results obtained he recommends this form of treatment. He states, however, that the variability of the results obtained by different authors is probably dependent on the different technique and different dosage as well as on the stage of the disease during which treatment is instituted. He is of the opinion that even in the cases where the foci in the multiple sclerosis cannot be influenced by direct roentgen rays, such an influence can be obtained indirectly through secondary rays. He believes that in this manner it is possible to influence favorably also very recent foci and very strongly radiosensitive cases without any danger to the individual. The fact that hitherto very few reports have appeared in the literature regarding unfavorable influence of the roentgen rays in cases of this type is due largely to the fact that up to now only old cases have been treated which are not strongly radiosensitive. A thorough knowledge of the subject is essential in order to obtain good results. If very large doses are given from the beginning, satisfactory results are obtained at first but the patient is thereby rendered radioresistant since the sclerotization of the focus is favorably influenced and the sclerotic focus is no longer as sensitive to the roentgen rays as the inflammatory focus. The author believes that best results could be obtained from a close cooperation between neurologists and roentgenologists in the treatment of cases of this type.—*A. Schwartzman.*

Horvath, Joseph. Die Röntgenbehandlung des Haut- und Lippenkarzinoms. (Roentgen treatment of carcinoma of the skin and lip.) *Strahlentherapie*, 1939, *65*, 216–236.

Between 1917 and 1935, 175 cases of carcinoma of the skin and lip were treated. In order to permit a comparable statistical evaluation of the results obtained, all skin epitheliomas, including carcinoma of the lip, were classified clinically, depending on the extent of the disease in four stages:

Stage 1. Small primary tumor localized at its point of origin, easily movable, which can be surgically removed with satisfactory cosmetic results. No regional or distant metastases.

Stage 2. The primary tumor, extended already to the underlying tissue, is still removable surgically but with poor cosmetic results. Regional or distant metastases are absent.

Stage 3. Considerable extension of the primary tumor with regional glandular metastases. Surgical removal practically hopeless.

Stage 4. Extensive inoperable primary tumor with extension into the neighboring organs; regional and distant metastases. In this group also cases were included where the primary tumor was small but where distant metastases were present.

Fifty-three cases, 25 males and 28 females, of the 175 cases treated belonged to Stage 1. In 37 cases primary irradiation could be carried out, while 16 cases were previously treated prior to admission. In 8 cases surgical treatment was carried out previously, in 7 cases the patient was irradiated and in one case surgery was followed by irradiation. Of the 53 cases of this group, 96.5 per cent were found free of symptoms, capable of doing their work after three years, 91.1 per cent after five years, 79.4 per cent after eight years, and 64.3 per cent after ten years.

Sixty-one of the 175 cases were of the second stage; 27 of these were males and 34 females. Primary irradiation could be carried out in only 32 cases, while the remaining 29 had some treatment prior to admission. Of these 61 cases, 63.9 per cent were perfectly well and free of symptoms after three years, 48.1 per cent after five years, 26.2 per cent after eight years and 21.2 per cent after ten years. Stages 3 and 4 were represented by 61 cases. Of these, 44 could be classified in Stage 3 and 17 in Stage 4; 32 of the patients were males and 29 females. In only 25 of these cases was the tumor still primary while in the remaining 36 there were local recurrences and metastases. Of these 61 cases freedom from symptoms and ability to work was obtained as follows: In 21.3 per cent after three years, in 12.9 per cent after five years, in 6.5 per cent after eight years and in 5.7 per cent after ten years. The author is of the opinion that these results compare very favorably with the results obtained by other methods of treatment.—*A. Schwartzman.*

Pagani, A. Die gutartigen Gefässgeschwülste der Parotisgegend und deren Behandlung mit Radiummoulage. (The benign vascular tu-

mors of the region of the parotid and their treatment with radium moulage.) *Strahlentherapie*, 1939, *65*, 204–215.

The present report is based on a study of 4 cases, children, suffering from vascular tumors in the region of the parotid gland. Three of these children came to observation during the first months of life. A histological diagnosis was made only in one case and was a capillary hemangioma of the parotid. The clinical picture and the satisfactory results obtained later with radium leave no doubt, however, that also in the remaining 3 cases not verified histologically the clinical diagnosis of hemangioma could not be doubted. The fourth patient, a child eight years of age, came to the author's observation seven years after the original removal of a tumor, interpreted as a lymphangioma, of the parotid region. Recurrences of this type are not rare and many authors are of the opinion that in hemangioma of this localization they can hardly be avoided. Contrary to the clinical assumption, however, histologically there was found in this case a cavernous hemangioma which apparently originated from the vessels of the periglandular tissue and secondarily extended to the parotid gland.

Benign vascular tumors of the parotid gland and of the region of the parotid are practically exclusively observed in infants and are recognized as such in a predominant number of cases during the first months of life. Just as the remaining vascular tumors, their origin is ascribed to embryonal disturbances and they are interpreted as a congenital, presumably hereditarily conditioned displacement of a vascular anlage. In favor of this view is the familial occurrence as well as the peculiar localization.

The clinical picture of hemangioma of the parotid gland and of the region of the parotid gland is characterized by a flat or semilunar tumor formation in the region of the parotid which in case of hemangioma appears somewhat bluish. The tumor is soft, compressible, grows rapidly at first, extending in most cases over the entire parotid gland and later assuming an infiltrative type of growth. Clinically it is difficult to differentiate lymphangioma from hemangioma. Clinically it is at times difficult to differentiate whether the angioma originates from the parotid gland proper or from the periglandular tissue. Histologically the capillary hyperplastic hemangioma of the parotid consists of well developed collapsed or blood-filled capillaries with delicate walls. Between the vessels there are found connective tissue septa. The endothelial cells of the vessels present at times an epithelium-like appearance and may also be stratified. Within the tumor tissue there may occasionally be found island-like remnants of glandular tissue.

In the 4 cases of the above-described type radium moulage was employed and very satisfactory results were obtained, both from the therapeutic and cosmetic viewpoints. The author recommends this method in preference to surgery because of the following considerations:

1. Complete painlessness of the treatment.
2. Applicability in childhood. This is especially important since the biological effect of radium is greatest on young growing tissue so that the treatment cannot be instituted too early.
3. With proper dosage splendid cosmetic results are obtainable.
4. The institution of early treatment in childhood prevents the possible later monstrous growth.—*A. Schwartzman.*

Pellegrini, G. Die Röntgentherapie der Schilddrüse bei der Behandlung der Dekompensation des Herzens. (Roentgen therapy of the thyroid gland in the treatment of cardiac decompensation.) *Strahlentherapie*, 1939, *65*, 330–343.

Roentgen irradiation of the thyroid gland of individuals suffering from circulatory insufficiency resulting from cardiac decompensation leads, as a rule, to a decrease of the utilization of oxygen so that the oxygen utilization is gradually brought to normal values, and later with repeated roentgen irradiation it is decreased from 10 to 25 per cent below normal. This decrease of the oxygen utilization may at first, that is, after the first two or three roentgen treatments, correspond to an improvement of the phenomena of decompensation and may later lead to a complete disappearance of the decompensation. In cases of more severe decompensation in association with very severe cardiac insufficiency, there appears only a slight improvement of the decompensation which does not persist after irradiation is stopped. But also in these cases the improvement, even though slight, is nevertheless significant. A physio-pathological study of the cardiac decompensation and its changes during and after roentgen irradiation of the thyroid gland shows

that as a result of the treatment the hyperthyroidism is decreased to normal or even subnormal values. This is of basic significance for the pathological sequelae of the dynamic biochemic and neuroendocrinological phenomena and represents a considerable part of the symptoms of circulatory insufficiency resulting from cardiac decompensation.

With the decrease of the hyperthyroidism the severe pathological symptoms gradually subside. In a predominant number of cases the heart becomes compensated; this, however, is not obtained in every case. When an equilibrium between a cardiac efficiency and the requirements of the peripheral circulation is achieved then the normalization of the circulation achieved by roentgen irradiation of the thyroid gland is not more stable than that obtained from the use of cardiac drugs. The oxygen utilization lowered by roentgen irradiation increases with the cessation of irradiation and remains at a given level as long as the requirements of the peripheral circulation do not disturb the equilibrium between this requirement and the maximum efficiency of the heart.

Roentgen irradiation has no contraindications, is practically without any danger which favorably contrasts with the use of cardiac agents, especially digitalization. Roentgen irradiation is especially indicated in the cases where digitalization is contraindicated or ineffective. It is also indicated in the cases where compensation cannot be achieved by means of digitalis; similarly it is indicated in the cases where the use of digitalis must be stopped because of a persistent bradycardia. A permanent improvement could not be expected in the cases where the cardiac insufficiency is of a type that a normal function of the circulation is not possible under a normal or subnormal oxygen utilization.

In contrast to the removal of the thyroid gland, roentgen irradiation of the thyroid gland has no contraindications. Its disadvantage in comparison with a thyroidectomy consists in the fact that a permanent improvement could not be expected in cases of persistent cardiac insufficiency in association with normal or subnormal oxygen utilization values.—*A. Schwartzman.*

Glauner, R., Teufel, S., and Daigger, A. Ergebnisse der protrahiert-fraktionierten Röntgenbestrahlung der Karzinome der oberen Luft- und Speisewege 1930 bis 1938. (Results from protracted fractional roentgen irradiation of carcinoma of the upper respiratory and food passages obtained from 1930 to 1938.) *Strahlentherapie* 1939, *65*, 397–408.

The protracted fractional method of irradiation of tumors of the upper air and food passages was employed by the authors in the course of the last eight years. In each case one field a day was irradiated, the individual dose varying from 120 to 240 r and the total dose usually divided over two lateral fields being equal to about 8,000 r. The general conditions of irradiation were usually 180 kv., 4 ma., 60 cm. focal skin distance, 1.2 mm. copper filter. The field size varied between 6×8 cm. and 10×15 cm. The individual as well as the total doses were adjusted to localization, general condition of the patient, reaction, etc.

All the cases treated in this manner are classified by the author in five groups, each group representing the following cases:

Group 1. Tumors of the mouth cavity comprising movable tumors of the gums, of the floor of the mouth, of the mucosa of the cheeks and of the alveolar processes as well as extensive carcinoma of the mouth cavity. There were no cases of carcinoma of the hard palate. Carcinoma of the lips was treated with radium and was not included here even when the regional glands were irradiated by the protracted fractional method. Tumors of the movable segment of the tongue were all inoperable.

Group 2 comprised tumors of the epipharynx and all were inoperable.

Group 3 was represented by tumors of the mesopharynx, that is, tumors of the soft palate and the uvula, of the tonsils, of the base of the tongue, as well as extensive mesopharynx tumors.

Group 4 comprised tumors of the hypopharynx, that is, all tumors of the external larynx, of the epiglottis, of the aryepiglottic folds, of the pyriform sinus as well as of the hypopharynx proper.

Group 5 comprised tumors of the inner larynx.

With the exception of some cases of Group 5, none of the treated tumors were operable.

On the basis of the results obtained, these authors come to the conclusion that also for the protracted fractional method of roentgen irradiation the law holds true that when a malig-

nant tumor has reached a certain size or when a malignant tumor extends beyond the point of its origin and has even involved the regional lymph glands, the prospects for a permanent cure are very slight. Even though in some cases treated in this manner a cure of three to five years' duration was obtained in spite of the involvement of the regional lymph nodes, this is explainable by unusually favorable circumstances such as very good radiosensitivity of the tumor and the possibility of a surgical removal of the involved regional lymph nodes. These authors come to the conclusion that the progress offered by protracted fractional irradiation is not as great as might be expected.—*A. Schwartzman.*

Wessely, Emil. Die Therapie des Karzinoms der Vallekula. (Therapy of carcinoma of the vallecula.) *Strahlentherapie*, 1939, *65*, 601–606.

Tumors in the region of the uvula and the lingual tonsils are somewhat different from the malignant tumors of the larynx and mouth because of their localization at the crossing point of the respiration and digestive tracts. During a certain stage of their development they lead to hoarseness, to mechanical interference with deglutition and during later stages to a considerable degree of dyspnea. In some instances decomposing tumors of this type give rise also to dysphagic conditions of a painful nature and at times to very severe salivation. In some cases tumors of this region are discovered only after they have given rise to regional glandular metastases and have reached such an extent that the asymmetry of the two sides of the neck can be recognized even at a distance. These glandular tumors are painful and up to a certain time do not give rise to any symptoms. Until recently surgery was the only method of treatment of this type of tumor. Surgery in cases of this type is rather extensive and it is technically difficult since it requires a partial resection of the larynx and of the root of the tongue or even a total resection of the root of the tongue. Unfortunately, however, in many instances regional metastases are already present even where they cannot as yet be detected by the palpating finger. Therefore, even extensive surgery does not give the desired results.

The modern method of treatment of tumors of this type is a combination of surgery and roentgen and radium treatment. Since 1932 this author treated 21 cases represented by 19 males and two females. The age of the patients varied between fifty and sixty years. The youngest was thirty-eight and the oldest was seventy-three years. Practically in each of the cases one had to deal with a flat epithelial carcinoma. In some instances the primary tumors were quite extensive and at times even presented extensive decomposition before revealing the presence of regional glandular metastases. In 12 cases there were found demonstrable glandular metastases which in some instances dominated the entire picture. All these tumors were treated roentgenologically by the method of Coutard. A dose of 4,500 r was given to two fields. The primary effect of the roentgen treatment was expressed in one form of a striking regression of the tumors during the second half of the irradiation period. In 7 cases no residual tumors remained. During the regression period, however, one is frequently surprised to find a remnant of the tumor at a point which could not be expected at first. Now such remnants of tumors are treated with radium. In one case the tumor originating from the epiglottis appeared somewhat refractory to the roentgen treatment but responded favorably to radium irradiation.

The author is of the opinion that tumors originating from the root of the tongue lead earlier to regional metastases than carcinoma originating from the epiglottis. The glandular metastases also show a great tendency to recurrence.

On the basis of the results obtained, the author states that the primary tumors in the region of the vallecula and of the lingual tonsils are in some instances exceptionally favorably influenced by roentgen treatment. In some cases additional radium therapy permits one to obtain satisfactory results where roentgen therapy appears ineffective. Even better results are obtainable in the cases where the glandular metastases are removed surgically and then roentgen rays and radium are given.—*A. Schwartzman.*

Reichenmiller, Hans. Individuelle Radiumbehandlung beim Krebs des Gabärmutterhalses. (Individual radium treatment in carcinoma of the uterine cervix.) *Strahlentherapie*, 1939, *65*, 595–600.

1. Experience based on a continuous observation of a large number of cases shows that the success of radiation treatment in carcinoma of

the uterine cervix depends basically on the effect of radium.

2. The rapid loss of the radium effect following its removal conditions chiefly the lack of results observed in some cases.

3. An elimination of the schematized standard method and an adjustment of the radium treatment to the actual extent of the carcinoma would assure better results. In cases where the carcinoma is very extensive, some of the carcinoma masses should be removed by means of a cold cautery so that the radium preparation can be introduced more closely to the marginal zone of the carcinoma.—*A. Schwartzman.*

Kirchhoff, Heinz. Die fraktionierte Röntgenbestrahlung fortgeschrittener Kollumkarzinome bei Mitbeteiligung der abführenden Harnwege. (Fractional roentgen irradiation of advanced carcinoma of the cervix with involvement of the efferent urinary passages.) *Strahlentherapie*, 1939, *65*, 579–594.

As a result of the anatomical position of the ureters, many diseases of the genital apparatus involve them directly or indirectly, leading to variable degrees of functional disturbances and at times even to complete urinary retention. The most frequent cause of death in carcinoma of the cervix is the ureteral involvement and its sequelae; the carcinomatous parametrial infiltrations surround and compress the ureter; at first there occurs a constriction with a proximal dilatation and later a complete occlusion. The slowly increasing surrounding of the ureters with the frequent perforation of the carcinoma into the external walls of the ureter leads clinically at first to oliguria, later to anuria and finally to uremic coma and death.

A systematic roentgen study of the urinary system of cases of carcinoma of the cervix reveals an unusually large number of congestion extending at times to conditions of hydroureter and hydronephrosis in a very large number of cases. Some authors are of the opinion that strictures of the ureters in cases of carcinoma of the cervix occur in about 50 per cent of the cases. Data of this type are usually based on studies of autopsy material.

Any intensive therapy, including radiation therapy of carcinoma, is associated with some danger. There is no uniformity of opinion regarding the primary morbidity and mortality following radiation treatment of carcinoma of the cervix. According to many authors the primary radium mortality varies from 2 to 4 per cent. The cause of death in these cases is peritonitis, pulmonary embolism and sepsis. According to the experience of this author, these complications represent 75 per cent of all cases where the treatment terminates lethally. Also the severe hemorrhage, the acute cardiac insufficiency, the rapidly progressing cachexia and the acute uremia following radium therapy play an important rôle. In 2 of the 16 primary radium mortalities observed in the radium treatment of 431 cases, death occurred as a result of acute uremic symptoms even though before irradiation there were no clinical signs of involvement of the urinary system. In both these cases the author had to deal with inoperable carcinoma of the cervix involving the parametrial tissues and as shown by the autopsy with strictures of the ureters resulting from tumor masses combined with hydroureter and hydronephrosis.

This author is of the opinion that insufficient attention has hitherto been paid to the involvement of the urinary organs in cases of carcinoma of the cervix. The author further believes that urinary complications frequently terminating lethally occurring during or after roentgen irradiation of the lesser pelvis are not as rare as it is generally assumed. In 20 of 152 cases treated by the original Coutard method, because of inoperable and incurable carcinoma of the cervix, the treatment was followed during irradiation by a severe aggravation of the general condition. There is no doubt that most of these cases would have died in any case, but not as rapidly. The aggravation of the general condition was manifested in the form of rapidly progressing cachexia, metastases, embolism and in 2 cases in uremia.

On the basis of these experiences the author comes to the following conclusions:

1. Before any radium or roentgen treatment of inoperable carcinoma of the cervix is instituted, a systematic study of the urinary apparatus must be carried out. This study must not be limited to cystoscopy and a determination of the non-protein nitrogen, but must include also roentgen examination of the urinary organs.

2. If a bilateral congestion of the excretory urinary system is found then extreme care is necessary even when minute doses of roentgen rays are used, because there is great danger of congestion of the already constricted ureters.

The congestion of the ureters is apparently the result of the appearance of edema of the mucosa of the ureters and increased pressure from outside due to an increase of the parametrial infiltration resulting in its turn from an inflammatory radiation exudate.

3. The relations are infinitely more satisfactory from the prognostic viewpoint when the congestion is unilateral. In cases of this type there is a possiblity that the healthy kidney takes over the function of the diseased kidney. This compensatory activity may be only transitory but nevertheless achieves its purpose.

4. Even in cases of unilateral congestion, however, one must consider the danger of a possible appearance of a reflex anuria of the healthy kidney. In such cases an immediate catheterization of the ureter is indicated.—*A. Schwartzman.*

Goecke, H. Unsere Behandlungsergebnisse beim Gebärmutterkrebs. (Results from the treatment of carcinoma of the uterus.) *Strahlentherapie*, 1939, *65*, 409–420.

Forty cases of carcinoma of the body of the uterus were treated by the author between 1925 and 1933. Of these, 29 cases, or 72.5 per cent, were operable and 11 cases, or, 27.5 per cent, were inoperable. The ratio of operability to inoperability in carcinoma of the body of the uterus is reversed as compared with that of carcinoma of the uterine cervix. Of the operable cases of carcinoma, 16 could be considered on the basis of five years' observation as cured. On this basis for the operable carcinoma of the body of the uterus a cure was therefore obtained in 55.1 per cent of the cases. Twelve cases were operated on and postoperatively irradiated while 17 cases were only irradiated. Of the first 12 cases 6, or 50 per cent, remained alive after five years while of the 17 cases 10, or 60 per cent, remained alive after five years.

The treatment carried out in cases of carcinoma of the body of the uterus was dependent on the age and general condition of the patient. Where surgery was carried out it was nearly always limited to a vaginal total extirpation of the uterus without the adnexa. The direct surgical mortality was zero. In each case following the operation a roentgen irradiation was given as well as a radium treatment.

A study of the 40 cases has shown that two-thirds of the treated cases were still alive after three years in the operable carcinoma of the body of the uterus while in the inoperable only about one-third of the cases were alive after three years.

During the same period, 263 cases of carcinoma of the cervix were treated. An absolute cure was obtained in 29.2 per cent of the cases, that is, after five years 77 of the 263 cases were still alive. Of the 263 cases of carcinoma of the cervix 80, or 30.4 per cent, could be classified as belonging to Groups I and II while 183 cases, or 69.6 per cent, were inoperable, that is, belonged to Groups III and IV. Of the 80 operable cases, 26 were operated on. The results obtained in the cases operated on and followed by irradiation were practically identical with the results obtained from irradiation only. The surgical mortality in the operated cases was 3.85 per cent. In conclusion, the author mentions the fact that a recurrence of a carcinoma of the cervix following operation or following irradiation is very unfavorable prognostically.—*A. Schwartzman.*

MISCELLANEOUS

Inouye, K. Biologische Wirkung von Alphastrahlen unter Berücksichtigung der Probleme der Radium-Schwachtherapie. (Biological effect of alpha rays in consideration of the problems of weak radium therapy.) *Strahlentherapie*, 1939, *64*, 175–200.

A series of studies has revealed the possibility that during the introduction of radium emanation into the organism the effects observed are ascribable not only to the direct influence of the incorporated emanation, but may be due also to the late effect of the products resulting from the emanation which has accumulated in the body. If these late products are deposited predominantly in the hemopoietic organs, then, in the presence of a sufficiently strong concentration, they may exert a continuous influence on the blood picture. Hitherto, however, no certain experimental basis for this possibility has been offered. Theoretically such a possibility can be conceived. An attempt was made by this author, therefore, to determine experimentally whether such products resulting from radium emanation accumulate in the body following radium introduction and, if so, how they are distributed in the individual organs. The experiments were carried out on rats and rabbits which were given daily in the course of a relatively long time, some radium

emanation in physiological salt solution in form of injections. After a number of weeks some of the animals died as a result of the effect of the incorporated radioactive substance while those which failed to die were killed and the tissues were then burned and their radium content determined. The results obtained from these studies may be briefly summarized as follows:

1. Following the introduction of radium emanation into the organisms sequel products which remain for a long time are actually deposited in the body.

2. The amount of the substances deposited in the body correspond to those which could be expected from theoretical computations.

3. Since the deposit of these substances takes place predominantly in the hemopoietic organs, it is quite conceivable that the late effects are dependent on the total amount of emanation introduced into the body. If the incorporated amounts of emanation are sufficiently large, the deposit of the sequel products may be sufficiently large to reach or even exceed the tolerance dose.

4. Special care must be exercised when preparations are used which contain not only radium emanation but also the radium salt in solution. A continuous use of preparations which give up relatively large amounts of radium salt in solution is associated with considerable danger.—*A. Schwartzman.*

Bade, Heinz, and Küntscher, Gerhard. Wirkungen von Röntgenstrahlen auf den Knochen. (Experimentelle Untersuchungen an Hunden.) (Action of roentgen rays on the bones; experimental studies on dogs.) *Fortschr. a. d. Geb. d. Röntgenstrahlen*, Sept., 1939, *60*, 235–242.

This study deals only with the bones as a supporting substance and not with their hematopoietic aspect. The first studies of this sort were carried out by Perthes in 1903 and the inhibitory effect of irradiation on growth was recorded. Further observations were made by Récamier, Försterling, Krukenberg, and others. In children, evidence is more difficult to obtain and the question usually arises as to whether the delay in growth was not caused by the disease for which the roentgen treatment was given. The same is true in adults where fractures occur in areas which have been previously irradiated. However, the authors believe that these fractures are often the so-called "fatigue" or "chronic" fracture and that the irradiation plays a direct rôle in their production. Salvetti (1914) was the first to observe the delayed healing of an experimental fracture in a rabbit under roentgen irradiation. Albee observed no effect, while Fukase found a favorable influence on callus formation in experiments on a large number of rabbits. Today most roentgenologists deny or are skeptical of the beneficial effect of irradiation on the healing of fractures. In recent years the experimental evidence is unanimous in the conclusion that irradiation can have only an inhibiting and never an accelerating action on the callus formation and osseous union.

In the authors' experiments it was not possible to produce "fatigue" fractures even after very high dosage. Although no change was demonstrable in the bone structure either by roentgen ray or by gross external examination, evidence of severe cellular damage was seen microscopically. Further studies in 5 dogs were carried out in which a piece 2 cm. long was resected from the left radius following irradiation of both forelegs. In all cases the wound healed promptly without infection. In the control dogs definite periosteal formation in the ulna occurred in two to three weeks and became marked in six weeks, while no such change was observed in the irradiated dogs. However, after four to eight weeks typical "fatigue" fractures appeared in the ulna opposite the site of the resection of the radius where irradiation had been applied. In no case did firm osseous union occur at the ulnar fracture site. Great care was taken to exclude the possibility of trauma and this evidence indicates that under some unusual stress pathological fractures will occur in bone which has been irradiated that would not occur otherwise.—*W. A. Evans, Jr.*

Gregori, Angelo. Wirkung von Röntgenstrahlen auf das Knochenmark "in vivo" and "in vitro." (The effect of roentgen rays on the bone marrow "in vivo" and "in vitro.") *Strahlentherapie*, 1939, *65*, 163–172.

The effect of roentgen rays on elements of bone marrow grown in vitro begins at a dose of about 10,000 r. Between a dose of 10,000 and 30,000 r the irradiated elements begin gradually to lose their ability of regeneration in the culture and gradually lose their movement ability until a standstill occurs. After this there appear in the cellular elements a series of destructive

necrobiotic phenomena which in some cases lead to death. After irradiation with a dose of 10,000 up to 20,000 r there appears on the second day in the irradiated cultures a decrease of the giant cells which present characteristics of megakaryocytes; these cells also appear in control cultures but somewhat later, about the fourth day. The premature appearance of these cells is apparently produced by the effect of the roentgen rays. A massive dose of 30,000 r destroys the irradiated culture immediately and completely.

While the dose necessary for the destruction of the bone marrow in vitro appears quite large the dose necessary for the destruction of the same cells in vivo is considerably smaller. On the fourth day following irradiation with 2,000 r the regeneration ability of the irradiated elements is decreased and in practically all cells irreversible necrobiotic phenomena appear. A piece of bone marrow irradiated with a massive dose of 6,000 r cultured four days after irradiation of the animal appears completely destroyed and presents also signs of a pronounced fatty degeneration. It appears, therefore, that the roentgen dose necessary for the destruction of the bone marrow cells in vivo is approximately eight to nine times smaller than that necessary for the destruction of the same cells in vitro. Following irradiation with doses of 2,000 to 3,000 r there appear larger numbers of fibroblast-like cells which apparently must be looked upon as transitional cells; megakaryocytes are rare. While irradiations with massive doses ranging from 1,000 to 5,000 r given in stages produce necrobiotic changes of the bone marrow cells, irradiation with 6,000 r leads predominantly to a strong fatty degeneration.—*A. Schwartzman.*

Sutro, Charles J., and Pomerantz, Leo. Effect of experimentally formed tumors on the musculoskeletal system of the rat. *Arch. Surg.*, June, 1939, *38*, 1132–1149.

Experimentally induced fibrosarcomas growing in tissues contiguous to skeletal parts did not show any marked tendency to invade the skeleton. When skeletal invasion did occur, it was via the joint capsule or by direct resolution of the cortex.

Tumors in the vicinity of the spinal cord, however, were associated with para-articular ossifications and skeletal abnormalities simulating the neurotrophic joint changes seen in man.—*P. J. Hodes.*

Harrington, H. L., and Huggins, Charles. Rate of removal of thorium dioxide from the blood stream. *Arch. Int. Med.*, March, 1939, *63*, 445–452.

The reticulo-endothelial system has been studied by injection of various substances such as bacteria, colloidal metals, quartz, carbon, egg yolk, egg albumin, bilirubin, and various dyes. The authors have made this analysis by using thorium dioxide, since with it, certain difficulties are avoided. Nine to 12 cc. of colloidal thorium dioxide (2.25 to 3 gm. of thorium dioxide) was injected into each of 19 normal dogs (weighing 8 to 20 kg.); 7 cc. of blood was withdrawn at frequent intervals and using a micromethod the thorium percentage was determined.

It was found that the rate of removal of the thorium was fastest during the first twenty minutes after injection and that it disappeared from the blood between ten and twelve hours, with the doses used. This rate of disappearance of thorium was not appreciably affected by anesthetics such as ether or pentobarbital sodium or by removal of the spleen or by bilateral nephrectomy. With removal of the pancreas and thereby the production of artificial diabetes, the rate of removal increased, thereby indicating that the lowered resistance on the part of diabetics is not due to deficient action of their reticulo-endothelial cells. With removal of as much as one-quarter of the liver, the rate of disappearance of the thorium from the blood was decreased.—*A. A. de Lorimier.*

Miyamoto, Sigeyuki. Experimentelle Sarkomerzeugung durch Thorotrast. (Experimental sarcoma production by thorotrast.) *Strahlentherapie*, 1939, *64*, 683–690.

A series of studies have been carried out by the author which have shown that in white rats thorotrast produces sarcoma with relative ease. As a rule, the sarcoma appears on the average after 321 days. There exists, however, a quite definite relationship between the latent period and frequency of the sarcoma development, on the one hand, and the dose of thorotrast employed on the other. The histologic studies have shown spindle cellular sarcoma tissue which has developed chiefly in the neighbor-

hood of the thorium granuloma. The transplantations always gave positive results and with one strain eleven inoculation passages were obtained. The histologic pictures of the inoculated tumors corresponded in general with those of the original tumors. The respiration and glycolysis of the tumor tissue fully harmonize with those of the malignant tumors. The rate of growth of the inoculated tumors did not present a definite value but in one of these tumors the rate of growth increased gradually after the last inoculation. The duration of life of the 7 surviving animals was on the average 63.4 days.—*A. Schwartzman.*

Toniolo, G. Wirkung der Röntgenstrahlen auf das Galliera-Sarkom in vivo und in vitro. (The effect of roentgen rays on Galliera sarcoma in vivo and in vitro.) *Strahlentherapie*, 1939, *65*, 375–396.

Before discussing the effect of roentgen rays on this type of sarcoma, the author enumerates the properties of the Galliera sarcoma as follows:

1. The tumor possesses a capsule and never shows a tendency to infiltrative growth.

2. When the tumor is inoculated into the skin, daughter tumors never appear either in the thoracic or in the abdominal viscera or in the lymph glands.

3. The transplants grow best in animals of about two months of age.

4. Inoculations carried out into the subcutaneous tissue which lead to the development of new growths in the thoracic and abdominal cavity permit no conclusions regarding any predilection for these particular regions.

5. Best results are obtained from an inoculation of a tumor tissue of about 0.5 cc. diluted with an equal amount of Ringer's solution.

6. Cases of regression are only rarely observed. In general, regressions occur in association with pregnancy of the inoculated animal. In no case, however, does a complete disappearance of the tumor occur. If the so-called pulp process is employed for purposes of inoculation, a take occurs in 100 per cent of the cases under the assumption, however, that one works with rats which are derived from the breed developed in the Experimental Station of Galliera in Genoa. At the end of the developmental processes of the tumor tissue, death occurs. At times recurrences on the margin of pressure ulcers appear.

The characteristic microscopic properties of Galliera sarcoma are as follows: One deals here with a sarcoma the parenchymal portion of which proliferates to such an extent that on a superficial examination the supporting tissue seems to be completely covered. Most of the cells are spindle shaped. The cellular components are made up of granulated protoplasmic spindles with a covered central segment, a vesicular nucleus and two fine processes. The carcoma frequently suggests the macro fusi-cellular type. Besides these cells there are frequently found in lesser numbers and in an irregular arrangement, plasma cells and polymorphous components; the latter comprise irregular polygonal, ovoid, round and at times very small cells similar to those found in a small cellular infiltration; at times the cells are somewhat larger and have an epithelioid appearance. Giant cells are present. The sarcoma contains numerous dilated capillaries filled with red blood corpuscles but there is no demonstrable definite wall structure of the capillaries.

A preceding treatment of the future sarcoma carriers (rats) by means of protein substances favors the development of the transplanted tumors.

Transplants of this type of sarcoma have a pure specific nature. In animals of another and even of a related type the experiments are negative.

A series of experiments was carried out by the author by means of the type of sarcoma described above and the results obtained are briefly summarized as follows:

The author studied the effect of roentgen rays on the infiltration and extension of the transplanted Galliera sarcoma in various stages of development as well as on the cells of a tissue pulp before the inoculation. He came to the following conclusions:

1. The same dose of roentgen rays which sterilizes the pulpy mass in the test tube destroys in a similar manner the tumor in an animal, however, only when one deals with a young tumor.

2. From the fifteenth day on, the radioresistance of the Galliera sarcoma gradually increases and after the thirtieth day practically no effect of the usual roentgen-ray dose is demonstrable.

3. If the filter is strengthened and the tension is increased then in vivo as well as in vitro lesser amounts of roentgen rays are necessary in order to obtain a sterilization of the sarcoma.

4. The disappearance of the tumor following irradiation or following an injection of sterilized tissue pulp apparently produces in the experimental animal no immunity towarts a new inoculation with the same tissue.—*A. Schwartzman.*

BADE, HEINZ. Die Röntgenstrahlenempfindlichkeit der Haut in Abhängigkeit vom zentralen und peripheren Nervensystem. (The roentgen-ray sensitiveness of the skin as dependent on the central and peripheral nervous systems.) *Strahlentherapie*, 1939, *66*, 50–65.

An experimental study of the effect of the central and peripheral nervous systems on the course of the radiation reaction of the skin of white rats was carried out. The biological test method, known as exudative radiodermatitis, was found very valuable in determining the radiation reaction of the shaved skin of rats.

Following a dose of 2,000 r and after a latent period of four or at the most, five days, the main reaction appears which presents a pronounced wave-like course. The intensity of the reaction is definitely increased and its apex is reached on the eighth or ninth day following the irradiation. At this time the irradiated field has become transformed into an ulcerative defect having distinctly demarcated borders. Histologically there is demonstrable a complete desquamation of the necrotic epidermis with a pronounced round cell infiltration of the subcutis. Beginning with the fourteenth day on healing sets in which begins from the margin, and the healing process is completed on the thirtieth day after the irradiation. The irradiated region is transformed into a fine delicate scar which remains permanently free of hair.

In similar experiments carried out on rats where the spinal cord was cut and as a result of which definite trophic changes of the paralyzed extremities appeared, the latent period was prolonged on the average to about ten days. In most of these animals the course of the reaction was also somewhat slower. Following a section of the anterior and posterior root of half of the body and the thereby produced peripheral paralysis of one posterior extremity there occurs a prolongation of the latent period to six to eight days. Also here in some cases a slowing of the course of the reaction could be observed. This author is of the opinion that the cause of the prolonged latent period and also of the frequently observed prolonged course of the reaction must be looked for in the circulatory disturbances of the paralyzed extremities conditioned by the central and peripheral paralysis.—*A. Schwartzman.*

BADE, HEINZ. Lässt sich ein Einfluss von Röntgenbestrahlungen, die die Toleranzgrenze der Haut nicht überschreiten, auf die quergestreifte Muskulatur nachweisen? (Is it possible to demonstrate an influence of roentgen radiation on striated musculature when the tolerance threshold of the skin is exceeded?) *Strahlentherapie*, 1939, *65*, 455–467.

Histological studies on irradiated musculature were carried out. In those following doses which led to a complete permanent epilation, no demonstrable morphological changes were found four days to two months after the irradiation was terminated. Rats following a single administration of 2,000 r without a filter at 180 or 60 kv. similarly showed no changes in the irradiated musculature. A dose of this type, however, leads to an ulcerative dermatitis of the skin which heals leaving a smooth scar; the connective tissue, however, and the musculature showed no changes during a space of time varying from four days to four weeks after the termination of the irradiation. The author had an opportunity to examine carefully one case of sarcoma of the shoulder blade. The infraspinatus muscle which received during the fractional irradiation a total of 3,000 r showed no morphological changes four weeks after the irradiation was terminated. A consecutive study of the creatine creatinine excretion and a determination of the blood values in 11 irradiated patients at the beginning and at the end of the series of irradiations showed no changes which would permit the conclusion that under the irradiation degenerative processes occur in the musculature. On the basis of these findings it may be stated that when the irradiation does not exceed the tolerance threshold of the skin severe injuries to the musculature are not to be expected.—*A. Schwartzman.*

LUTHER, WOLFGANG. Die Wirkung der Röntgenstrahlen auf die Zellteilung. (The effect of roentgen rays on cell division.) *Strahlentherapie*, 1939, *66*, 40–49.

The radiation reaction of living tissue varies depending on the type of the irradiated cells and on the method of irradiation. This differ-

ence may be due to the fact that the sensitiveness or the restoration ability of the individual types of cells vary; on the other hand, it may be due to the fact that, in the same cell numerous processes are incited by the irradiation and these processes take a course independently of each other, the effects of which may partly interrupt each other. Depending on the conditions of the individual case either one or the other of these processes predominates and thereby determines the external visible course of the radiation effect in the tissue. When an attempt is made to carry out experiments, using different methods and different objects and to compare the results obtained, in order to derive some generally applicable laws, it is essential to remember the reaction abilities of the cell in general which exist in the given experimental arrangement and which respond in a given manner to the radiation stimulus.

The purpose of this work is to show that in the irradiated tissue at least two different radiation effects may appear, both of which affect the division mechanism of the cell but which apparently are not directly related to each other. The experiments of this author were carried out on the *Salamandra maculosa L.* The radiation effect on the skin of these larvae presents a very characteristic course. Irradiations with doses varying from 500 to 1,000 r are at first apparently tolerated without any reaction. The animals remained completely healthy as long as they remained in water. As soon as the larvae leave the water there appears immediately and suddenly a severe skin injury which leads to death in a relatively short time. The transformation of the larval skin to the spotted epidermis of the terrestrial salamander is delayed. When doses exceeding 600 r are used no metamorphosis of the skin takes place. The epidermis is discarded so that the subcutaneous tissue becomes exposed and the animals die as a result of infection. Doses below 500 r are, as a rule, not lethal. Even here, however, the characteristic spotting is highly disturbed and the irradiated skin is also thinner and poorer in glands than the skin of the non-irradiated animals.

The outstanding characteristic of this skin reaction is the fact that its time of appearance is independent of the size of the dose or of the method of irradiation but is dependent on the appearance of the metamorphosis. When the metamorphosis is artificially made to appear earlier, then also the radiation injury appears earlier, and vice versa. In cases of this type we no longer deal with a latent period in the proper sense of the word, but with a type of late injury or with a combination injury which appears only when as a result of special functions, such as transformation into the terrestrial form, the skin is overburdened.

A series of experiments was carried out in order to determine the nature of the skin injury described above and it was found that the injury occurs not as a result of a disturbance in the course of the cell division, but as a result of a blockade of the cell division ability in general, that is, a large number of old cells become in general incapable of cell division, and this disturbance is permanent when the dose exceeds a certain level, in the case studied when the dose exceeds 500 or 600 r. This dose does not influence the vegetative functions of the skin and, therefore, there do not appear at first any externally visible effects because the use of the skin during the larval life in water is only slight. With the transition to terrestrial life, however, the function of the skin is increased and as a result of this increase in function the changes become visible because of the blockade of the cell division.—*A. Schwartzman.*

Langendorff, H., and Papperitz, W. Über die Wirkung einer einzeitig verabreichten Röntgendosis auf das Knochenmark der weissen Maus. (The effect of a single roentgen dose on the bone marrow of a white mouse.) *Strahlentherapie*, 1939, *65*, 624–629.

In a previous communication the authors reported that in plant as well as in animal tissue irradiation with short wave rays leads to the appearance of a reaction mechanism characterized by a wave-like course distinct for the tissue studied. An attempt was made in this study to determine whether tissues made up of different structural elements show the same or similar courses of reaction as those mentioned previously. To determine this possibility the behavior of the bone marrow was analyzed more closely; bone marrow was employed because of its structure and its great radiosensitiveness. Studies were carried out on white male mice three months of age, free of infection and otherwise appearing perfectly healthy. The animals were irradiated with one dose of 400 r, with 180 kv. and 4 ma. The bone marrow was examined in sections and in each case a thor-

ough and careful study of the blood picture was made before and after irradiation.

These studies have shown that nine hours after irradiation definite changes occur in the bone marrow which terminate after two to two and one-half hours. The changes are expressed in the form of a definite nuclear decomposition in various cellular forms which may begin in some cases two to three hours after irradiation. Shortly afterward the regeneration phase appears. It reaches its highest point twenty days after irradiation and manifests itself in the form of appearance of numerous mitotic figures in the bone marrow. The course of the leukopoiesis appears to be the most outstanding manifestation of the reaction curve. Also the erythropoiesis is influenced by irradiation but in the curve this influence is manifested only on the twelfth day after irradiation. The study has further shown that each cellular form presents a reaction curve characteristic of it. Immediately after irradiation there occurs a definite injury to the lymphocytes as a result of which the number of lymphocytes is decreased. Parallel with this there occurs an increase in the neutrophilic leukocytes which leads to the well known picture of the essential luekocytosis appearing three hours after irradiation. Even at this time, however, there are already present signs of injury to the cells expressed in form of excessive segmentation of the nuclei. During the following two hours there occurs a decrease in the number of all white blood cells. After twenty-four hours there occurs an elevation in the number of neutrophilic leukocytes. At the same time a monocytosis is demonstrable in the blood.

In conclusion, the authors state that even after a single roentgen irradiation the effect on the bone marrow of the white mouse can be demonstrated in the form of qualitative and quantitative changes which take place in all blood building cellular forms. Also here there occurs a wave-like radiation reaction in which a primary, secondary and tertiary effect can be differentiated.—*A. Schwartzman.*